10591921

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 12	Match STN Content and Features to Your Information Needs, Quickly and Conveniently
NEWS	3	JAN 25	Annual Reload of MEDLINE database
NEWS	4	FEB 16	STN Express Maintenance Release, Version 8.4.2, Is Now Available for Download
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NEWS	6	FEB 16	New FASTA Display Formats Added to USGENE and PCTGEN
NEWS	7	FEB 16	INPADOCDB and INPAFAMDB Enriched with New Content and Features
NEWS	8	FEB 16	INSPEC Adding Its Own IPC codes and Author's E-mail Addresses
NEWS	9	APR 02	CAS Registry Number Crossover Limits Increased to 500,000 in Key STN Databases
NEWS	10	APR 02	PATDPAFULL: Application and priority number formats enhanced
NEWS	11	APR 02	DWPI: New display format ALLSTR available
NEWS	12	APR 02	New Thesaurus Added to Derwent Databases for Smooth Sailing through U.S. Patent Codes
NEWS	13	APR 02	EMBASE Adds Unique Records from MEDLINE, Expanding Coverage back to 1948
NEWS	14	APR 07	CA/CAplus CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
NEWS	15	APR 07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAplus
NEWS	16	APR 07	MEDLINE Coverage Is Extended Back to 1947

NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,
AND CURRENT DISCOVER FILE IS DATED 15 JANUARY 2010.

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Enter NEWS followed by the item number or name to see news on that specific topic.

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and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:06:12 ON 04 JUN 2010

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND
command can only be used to look at the index in a file which has an
index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'REGISTRY' ENTERED AT 10:06:35 ON 04 JUN 2010
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 2 JUN 2010 HIGHEST RN 1226851-61-1
DICTIONARY FILE UPDATES: 2 JUN 2010 HIGHEST RN 1226851-61-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

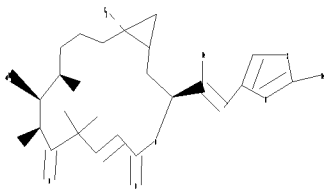
TSCA INFORMATION NOW CURRENT THROUGH January 8, 2010.

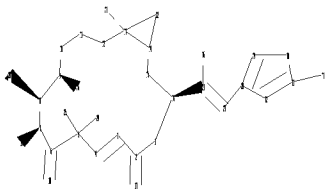
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10591921z.str





chain nodes :
17 18 19 20 21 23 24 25 26 27 33 36
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 22 28 29 30 31 32
chain bonds :
2-17 5-24 5-25 6-18 7-19 8-20 9-26 13-23 16-21 21-27 21-36 27-28 31-33
ring bonds :
1-2 1-16 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14
13-22 14-15 14-22 15-16 28-29 28-32 29-30 30-31 31-32
exact/norm bonds :
2-17 6-18 8-20 13-23 28-32 31-32
exact bonds :
1-2 1-16 2-3 3-4 4-5 5-6 5-24 5-25 6-7 7-8 7-19 8-9 9-10 9-26 10-11
11-12 12-13 13-14 13-22 14-15 14-22 15-16 16-21 21-27 21-36 27-28 28-29
29-30 30-31 31-33
isolated ring systems :
containing 1 : 28 :

G1:H,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:Atom 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:CLASS 36:CLASS

Stereo Bonds:

19-7 (Single Hash).
20-8 (Single Wedge).
21-16 (Single Wedge).
26-9 (Single Hash).

Stereo Chiral Centers:

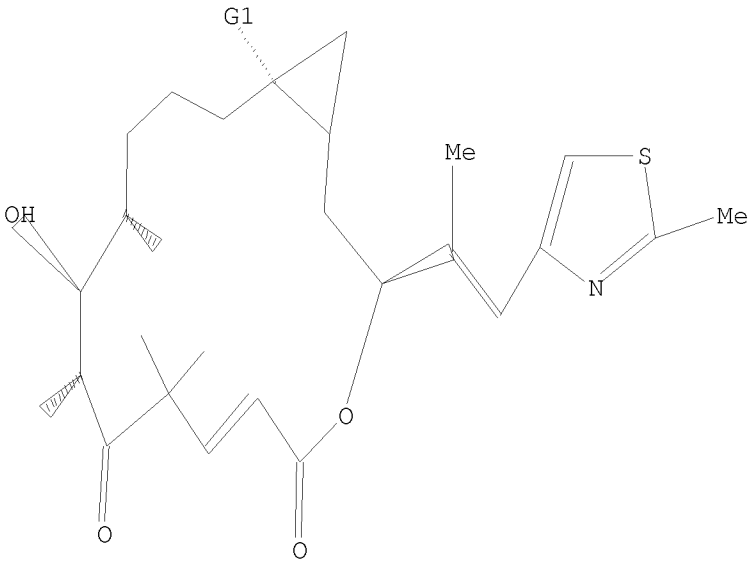
7 (Parity=Even)
8 (Parity=Odd)
9 (Parity=Odd)
16 (Parity=Even)

Stereo RSS Sets:

Type=Relative (Default). 4 Nodes= 7 8 9 16

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

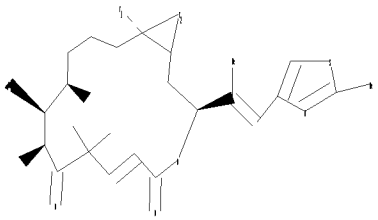


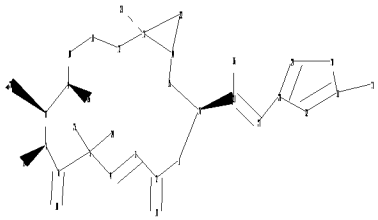
G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1

```
SAMPLE SEARCH INITIATED 10:06:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       45 TO ITERATE

100.0% PROCESSED       45 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          498 TO     1302
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 10:07:07 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      897 TO ITERATE

100.0% PROCESSED      897 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L3            0 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\10591921z1.str
```





```
chain nodes :
17  18  19  20  21  23  24  25  26  27  33  36
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  22  28  29  30  31  32
chain bonds :
2-17  5-24  5-25  6-18  7-19  8-20  9-26  13-23  16-21  21-27  21-36  27-28  31-33
```

ring bonds :
1-2 1-16 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14
13-22 14-15 14-22 15-16 28-29 28-32 29-30 30-31 31-32
exact/norm bonds :
1-2 1-16 2-3 2-17 3-4 4-5 5-6 5-24 5-25 6-7 6-18 7-8 7-19 8-9 8-20
9-10 9-26 10-11 11-12 12-13 13-14 13-22 13-23 14-15 14-22 15-16 16-21
21-27 21-36 27-28 28-29 28-32 29-30 30-31 31-32 31-33
isolated ring systems :
containing 1 : 28 :

G1:H,Ak

G2:C,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:Atom 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:CLASS 36:CLASS

Stereo Bonds:

19-7 (Single Hash).
20-8 (Single Wedge).
21-16 (Single Wedge).
26-9 (Single Hash).

Stereo Chiral Centers:

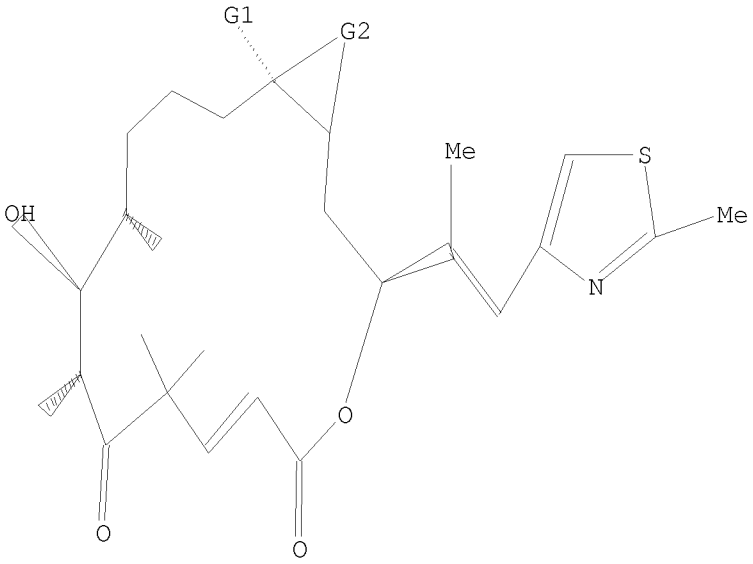
7 (Parity=Even)
8 (Parity=Odd)
9 (Parity=Odd)
16 (Parity=Even)

Stereo RSS Sets:

Type=Relative (Default). 4 Nodes= 7 8 9 16

L4 STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4 STR



G1 H,Ak

G2 C,O

Structure attributes must be viewed using STN Express query preparation.

```
=> s l4
SAMPLE SEARCH INITIATED 10:09:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       45 TO ITERATE

100.0% PROCESSED       45 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          498 TO     1302
PROJECTED ANSWERS:               0 TO        0

L5            0 SEA SSS SAM L4

=> s l4 sss full
FULL SEARCH INITIATED 10:09:47 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      779 TO ITERATE

100.0% PROCESSED      779 ITERATIONS                               6 ANSWERS
SEARCH TIME: 00.00.01

L6            6 SEA SSS FUL L4

=> FIL HCAPLUS
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   385.04     385.26
```

FILE 'HCAPLUS' ENTERED AT 10:09:55 ON 04 JUN 2010

FILE COVERS 1907 - 4 Jun 2010 VOL 152 ISS 24
FILE LAST UPDATED: 3 Jun 2010 (20100603/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2010
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2010

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2010.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

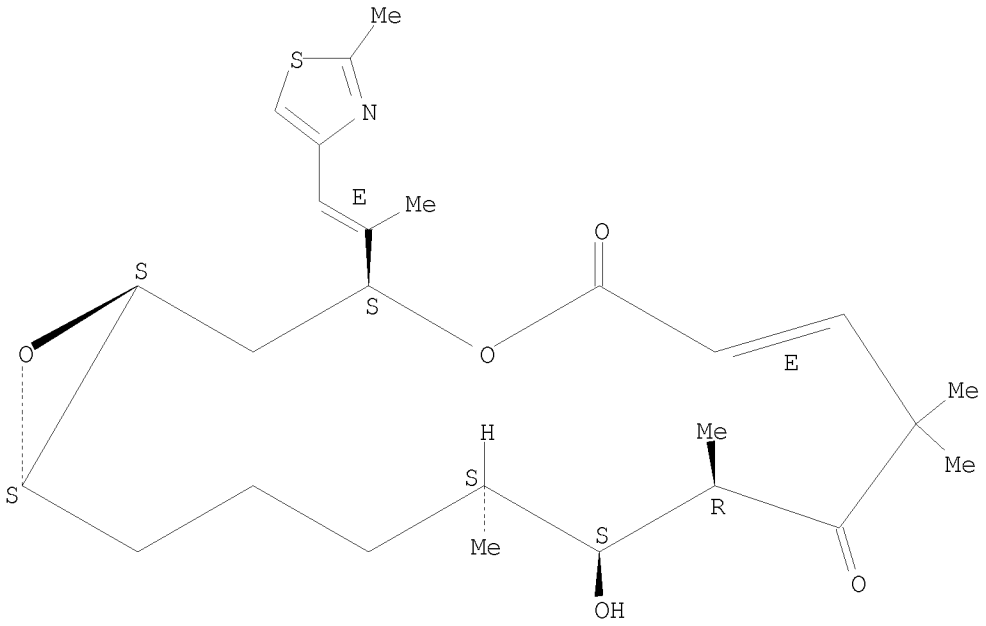
This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s l6
L7          19 L6

=> s l7 and py<=2004
      25158292 PY<=2004
L8          17 L7 AND PY<=2004

=> d l7 ibib abs hitstr tot
```

L7 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2008:1383637 HCAPLUS
DOCUMENT NUMBER: 149:555127
TITLE: Dioxirane epoxidation of alkenes
AUTHOR(S): Adam, Waldemar; Saha-Moeller, Chantu R.; Zhao, Cong-Gui
CORPORATE SOURCE: Universitaet Wuerzburg, Wuerzburg, Germany
SOURCE: Organic Reactions (Hoboken, NJ, United States) (2002), 61, No pp. given
CODEN: ORHNBA
URL: http://www3.interscience.wiley.com/cgi-bin/mrwhome/107610747/HOME
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 149:555127
AB A review of the article Dioxirane epoxidn. of alkenes.

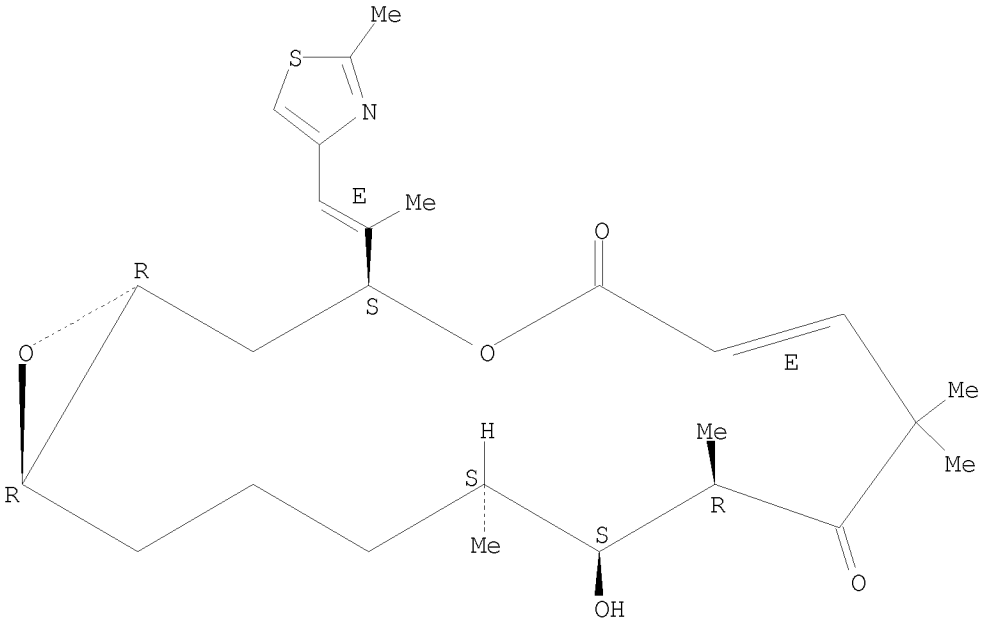
IT 193071-71-5P 193071-72-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(Dioxirane Epoxidn. of Alkenes)
RN 193071-71-5 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

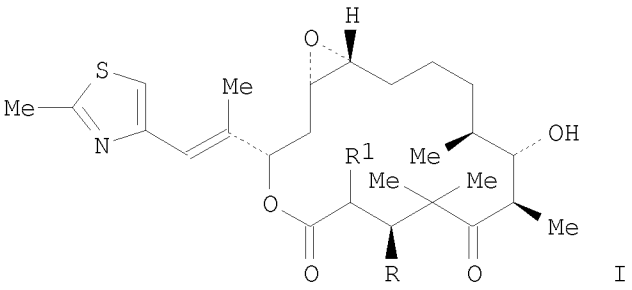


RN 193071-72-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L7 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2008:191355 HCAPLUS
DOCUMENT NUMBER: 148:355544
TITLE: Conformational Preferences of Natural and C3-Modified Epothilones in Aqueous Solution
AUTHOR(S): Erdelyi, Mate; Pfeiffer, Bernhard; Hauenstein, Kurt; Fohrer, Joerg; Gertsch, Juerg; Altmann, Karl-Heinz; Carlomagno, Teresa
CORPORATE SOURCE: NMR-Based Structural Biology, Max-Planck-Institute for Biophysical Chemistry, Goettingen, D-37077, Germany
SOURCE: Journal of Medicinal Chemistry (2008), 51(5), 1469-1473
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 148:355544
GI



I

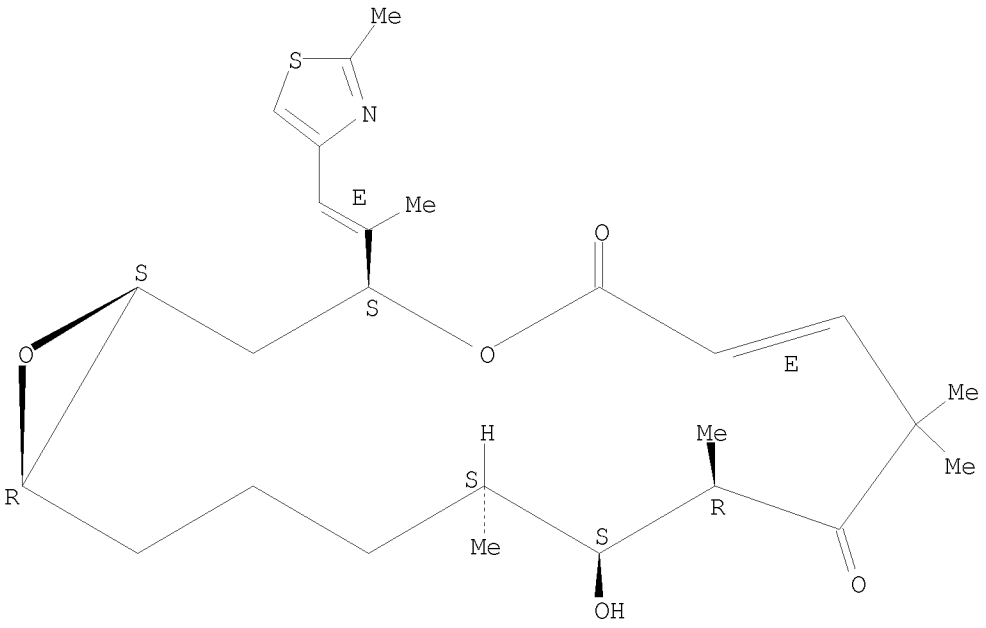
AB The conformational properties of the microtubule-stabilizing agent epothilone A (I, R = OH, R1 = H) and its 3-deoxy and 3-deoxy-2,3-didehydro derivs. I (R = R1 = H) and I (RR1 = E-bond) have been investigated in aqueous solution by a combination of NMR spectroscopic methods, Monte Carlo conformational searches, and NAMFIS calcns. The tubulin-bound conformation of epothilone A, as previously proposed on the basis of solution NMR data, was found to represent a significant fraction of the ensemble of conformations present for the free ligands in aqueous solution

IT 476623-83-3P
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(conformational preferences of epothilone A and 3-deoxy derivs. in aqueous solution and antitumor activity)

RN 476623-83-3 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

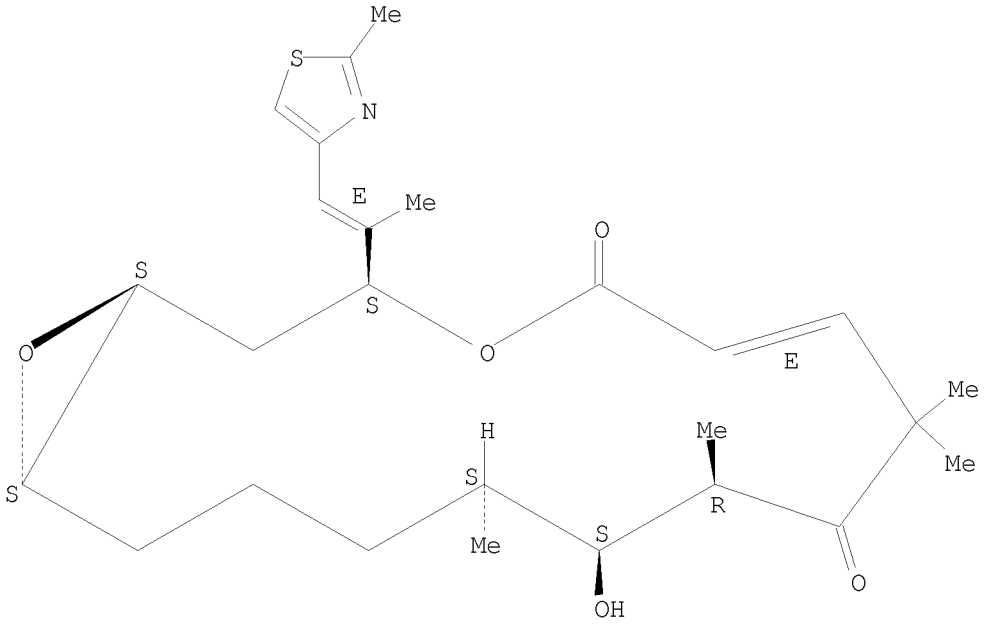


OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2006:396881 HCAPLUS
DOCUMENT NUMBER: 145:240913
TITLE: Prediction of antitumor activity for epothilone

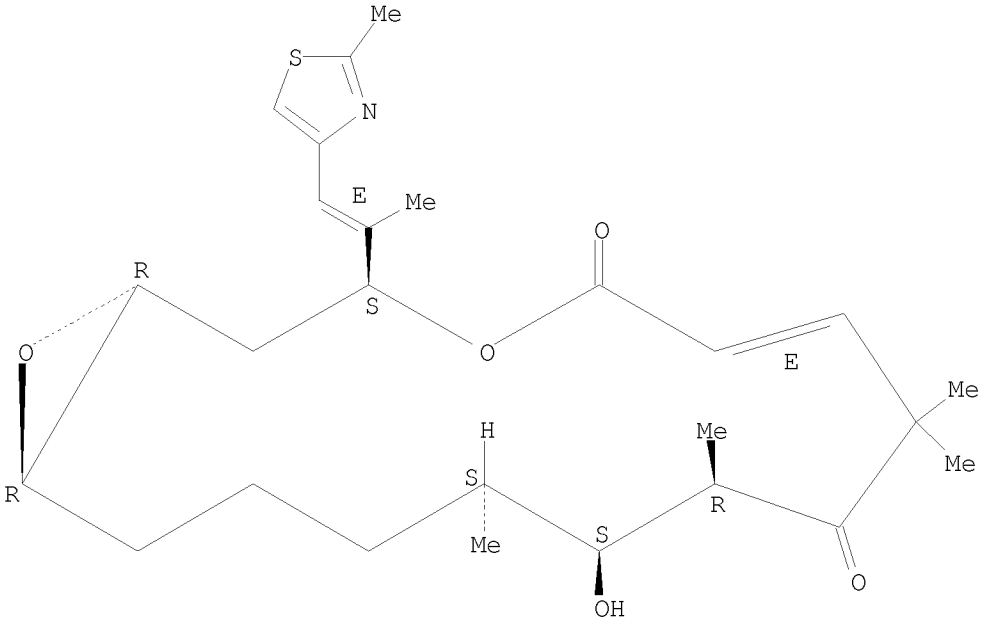
analogues based on 3D molecular descriptors
AUTHOR(S): Tan, Ning-Xin; Li, Juan-Qin; Li, Ze-Rong; Li, Xiang-Yuan
CORPORATE SOURCE: Coll. Chem. Eng., Sichuan Univ., Chengdu, 610065, Peop. Rep. China
SOURCE: Wuli Huaxue Xuebao (2006), 22(4), 397-402
CODEN: WHXUEU; ISSN: 1000-6818
PUBLISHER: Wuli Huaxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB In order to predict the antitumor activities of various epothilone analogs, a set of mol. descriptors, including electronic, topol. and geometric descriptors, and mol. shape indexes (K-order moment shape indexes), were calculated to characterize the structural and physicochem. properties for 150 compds. The 30 descriptors selected with genetic algorithm were employed to establish the classification and prediction model of epothilone analogs by using support vector machine(SVM). This SVM system gives a total prediction accuracy of 83.3% by the leave-one-out method and that of 80.6% by the 5-fold cross-validation method. The present study indicates that K-order moment shape indexes are useful for description of configuration isomers, and SVM is a facilitating tool in prediction of antitumor activity of epothilone analogs.
IT 193071-71-5 193071-72-6
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prediction of antitumor activity for epothilone analogs based on 3D mol. descriptors)
RN 193071-71-5 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193071-72-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

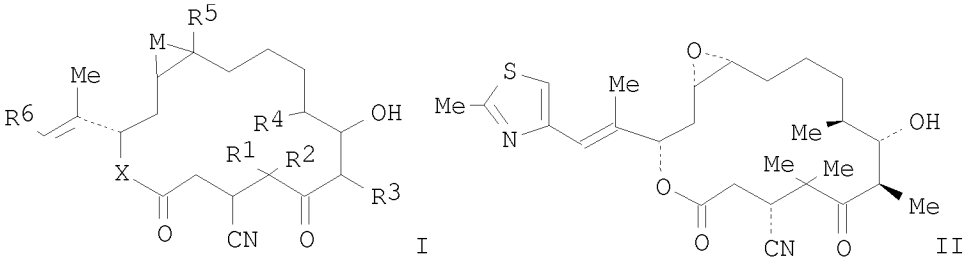
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L7 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2003:757689 HCAPLUS
DOCUMENT NUMBER: 139:276755
TITLE: Preparation of epothilone derivatives for therapeutic use as anticancer agents
INVENTOR(S): Regueiro-Ren, Alicia; Kim, Soong-Hoon
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078411	A1	20030925	WO 2003-US7584	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003218110	A1	20030929	AU 2003-218110	20030311
US 20030191089	A1	20031009	US 2003-386072	20030311
US 6719540	B2	20040413		
EP 1483251	A1	20041208	EP 2003-714096	20030311
EP 1483251	B1	20091223		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 452896	T	20100115	AT 2003-714096	20030311
PT 1483251	E	20100226	PT 2003-714096	20030311
ES 2337134	T3	20100421	ES 2003-714096	20030311

PRIORITY APPLN. INFO.: US 2002-363441P P 20020312
WO 2003-US7584 W 20030311
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 139:276755
GI

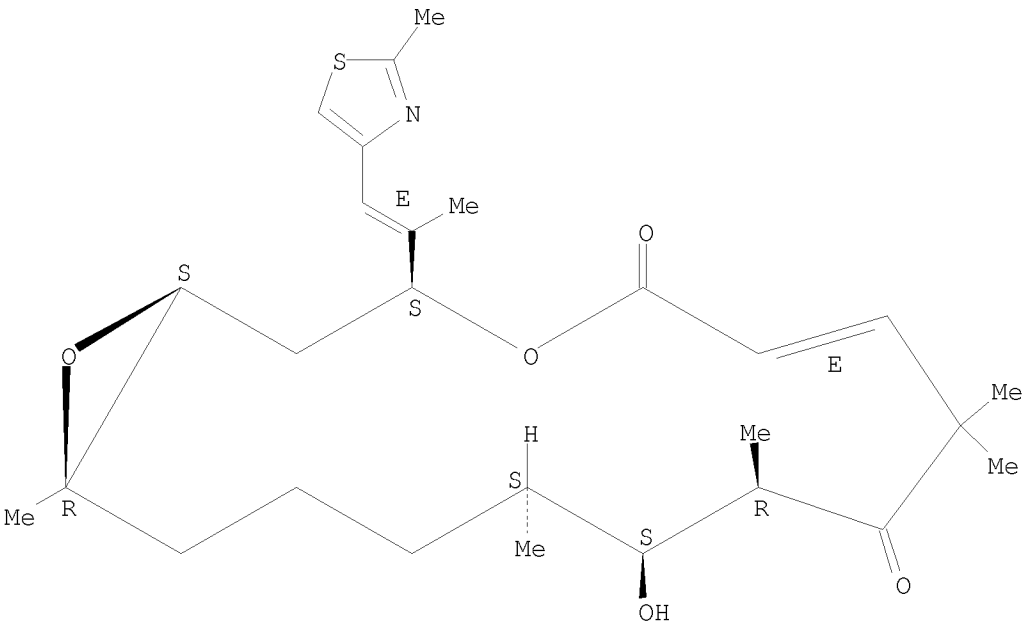


AB Epothilone derivs., such as I [M = bond, O, NR9, CR10R11; X = O, NH; R1-R4 = H, alkyl; R5 = H, alkyl, cyano; R6 = H, alkyl, aryl, heterocyclyl; R9-R11 = H, OH, alkyl, alkoxy, aryl, cycloalkyl, heterocyclyl], pharmaceutically acceptable salts, solvates or hydrate thereof, were prepared for use as antitumor agents. Thus, epothilone derivative II was prepared from 2,3-dehydro epothilone A, via silylation of hydroxyl group, potassium cyanide addition, followed by deprotection. The prepared epothilone derivs. were assayed in vitro for their effect on tubulin polymerization and for cytotoxicity against HCT-116 human colon carcinoma cells. Therapeutic compns. containing I or in combination with other therapeutic agents useful in the treatment of cancer or other proliferative diseases are also claimed.

IT 226956-21-4 476623-83-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of epothilone derivs. for therapeutic use as anticancer agents)

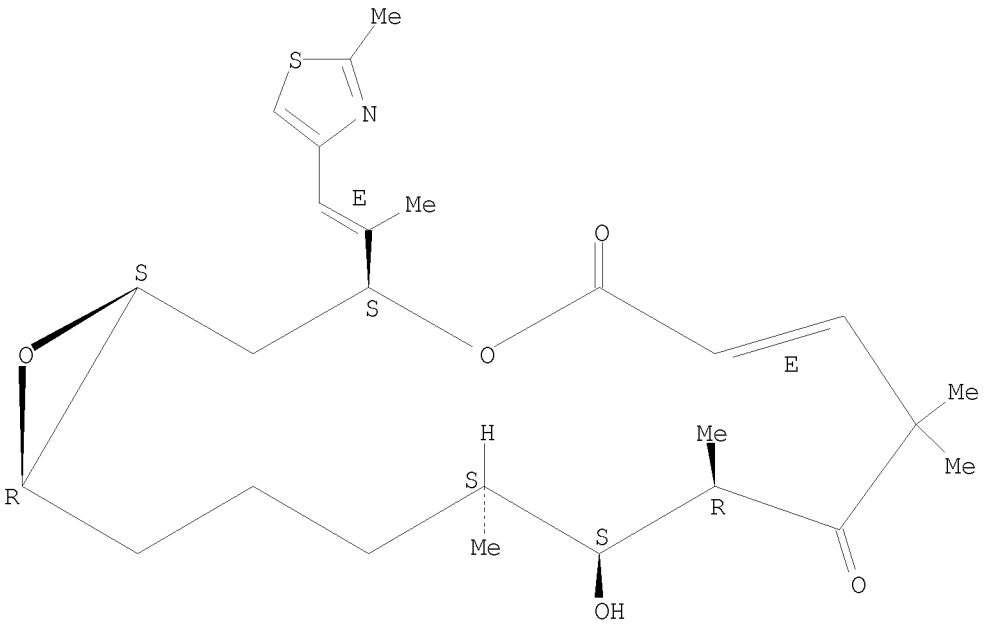
RN 226956-21-4 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 476623-83-3 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

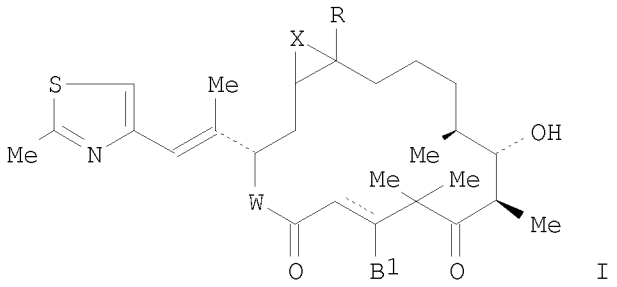
L7 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:946278 HCAPLUS
DOCUMENT NUMBER: 138:24591
TITLE: Preparation of epothilone derivatives for therapeutic use as anti-cancer agents
INVENTOR(S): Regueiro-Ren, Alicia; Borzilleri, Robert M.; Vite, Gregory D.; Kim, Soong-Hoon
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098868	A1	20021212	WO 2002-US15397	20020514

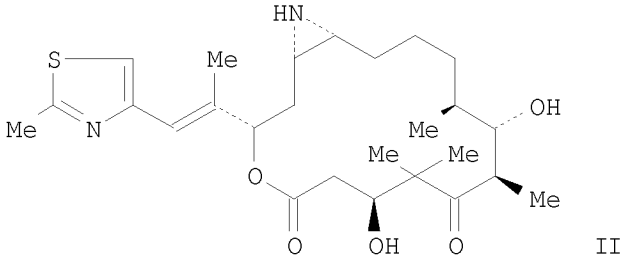
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2449077	A1	20021212	CA 2002-2449077	20020514
AU 2002309843	A1	20021216	AU 2002-309843	20020514
US 20030087888	A1	20030508	US 2002-144879	20020514
US 6800653	B2	20041005		
EP 1392664	A1	20040303	EP 2002-736867	20020514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004532888	T	20041028	JP 2003-501991	20020514
MX 2003010909	A	20040217	MX 2003-10909	20031127
PRIORITY APPLN. INFO.:			US 2001-295499P P	20010601
			WO 2002-US15397 W	20020514

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 138:24591
GI



I



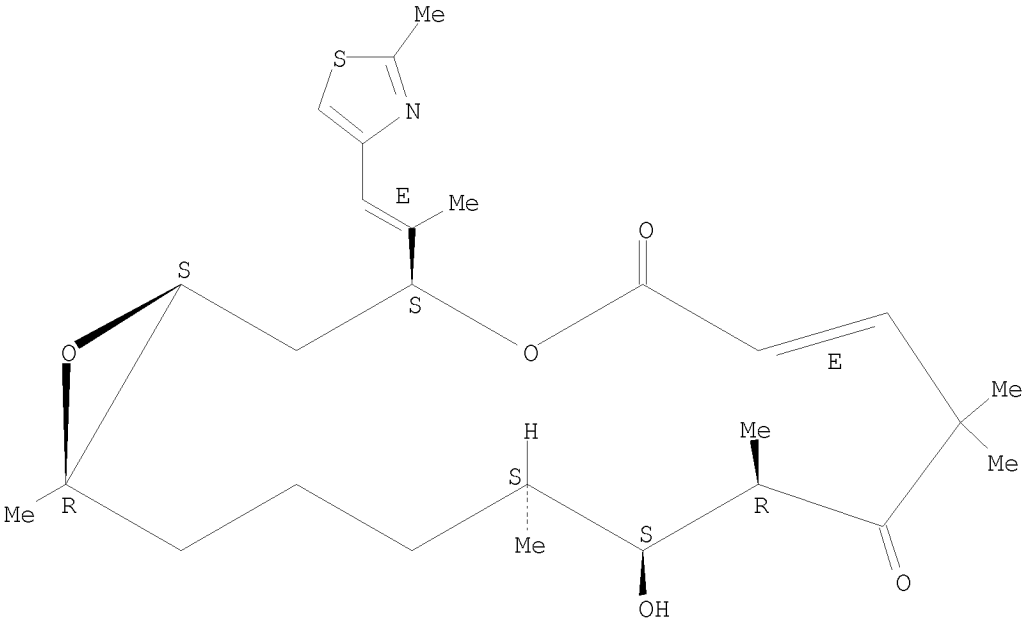
II

AB Epothilone derivs., such as I [B1 = H, OH, alkoxy, acyloxy, carbamoyl, etc.; W = O, S, NR16; X = O, S, CO, SO, SO2, CH2, CCl2, CBr2, NR1, etc.; R1 = H, alkyl; R16 = H, alkyl, aryl, cycloalkyl, heterocyclyl, etc.], were prepared for use as antitumor agents. Thus, aza-epothilone derivative II via a series of synthetic steps which included epoxidn. of epothilone C using 0.0004 M Na2EDTA, F3CCOMe, 2KHSO5.KHSO4.K2SO4 (potassium peroxymonosulfate) and NaHCO3 in MeCN to form epothilone A and 12,13-diepi-epothilone A in 57 and 29% yields, resp., followed by epoxide ring opening/azidation of 12,13-diepi-epothilone A using NaN3 and NH4Cl in EtOH to form the azido-hydroxy derivative in 59% yield, and, finally, formation of II in 62% yield using PPh3 and heating the azido-hydroxy derivative at 60° for 14 h. in THF. The prepared epothilone derivs. were assayed in vitro for their effect on tubulin polymerization and for cytotoxicity against HCT-116 human colon carcinoma cells.

IT 226956-21-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone derivs. for therapeutic use as anti-cancer agents)
RN 226956-21-4 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:760736 HCAPLUS
DOCUMENT NUMBER: 138:95
TITLE: SAR and pH Stability of Cyano-Substituted Epothilones
AUTHOR(S): Regueiro-Ren, Alicia; Leavitt, Kenneth; Kim, Soong-Hoon; Hoefle, Gerhard; Kiffe, Michael; Gougoutas, Jack Z.; DiMarco, John D.; Lee, Francis Y. F.; Fairchild, Craig R.; Long, Byron H.; Vite, Gregory D.
CORPORATE SOURCE: Divisions of Discovery Chemistry Oncology Drug Discovery and Pharmaceutical Development, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-4000, USA
SOURCE: Organic Letters (2002), 4(22), 3815-3818
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society

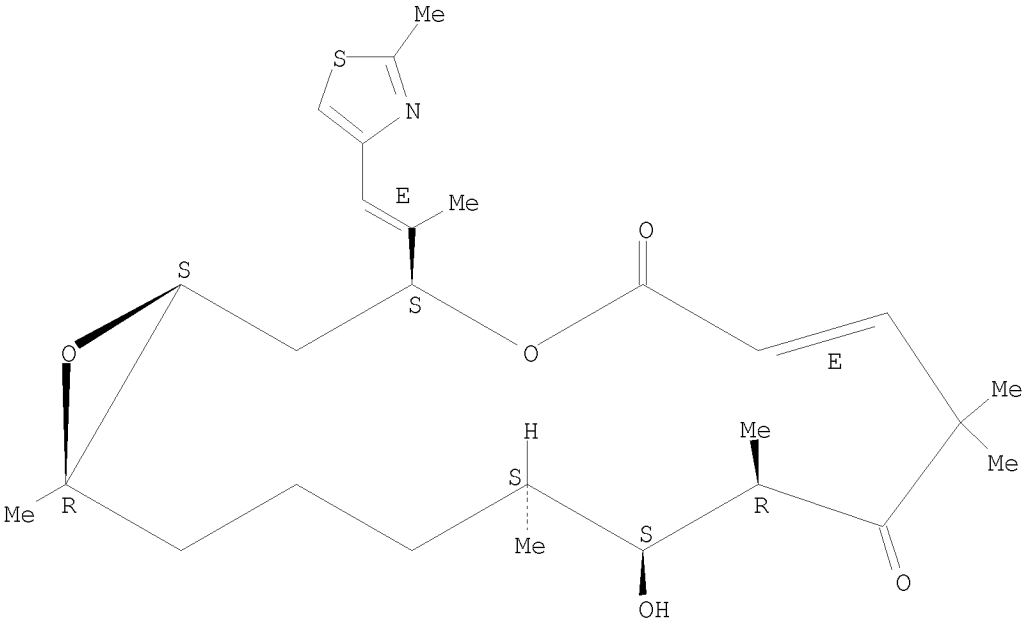
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:95

AB 3-Cyano epothilones are the examples of non-hydroxy C-3-substituted analogs. Their tubulin binding affinity and cytotoxicity provide meaningful structure-activity relationship information on the dependence of C-1/C-3 conformation upon activity. 12-Cyano epothilone has improved pH stability over epothilone B, and its activity further supports the hypothesis that C-12 stereochem. is not critical for tubulin affinity.

IT 226956-21-4P 476623-83-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(pH stability, preparation and structure-activity relationship of cyano-substituted epothilones in human colon carcinoma cells)

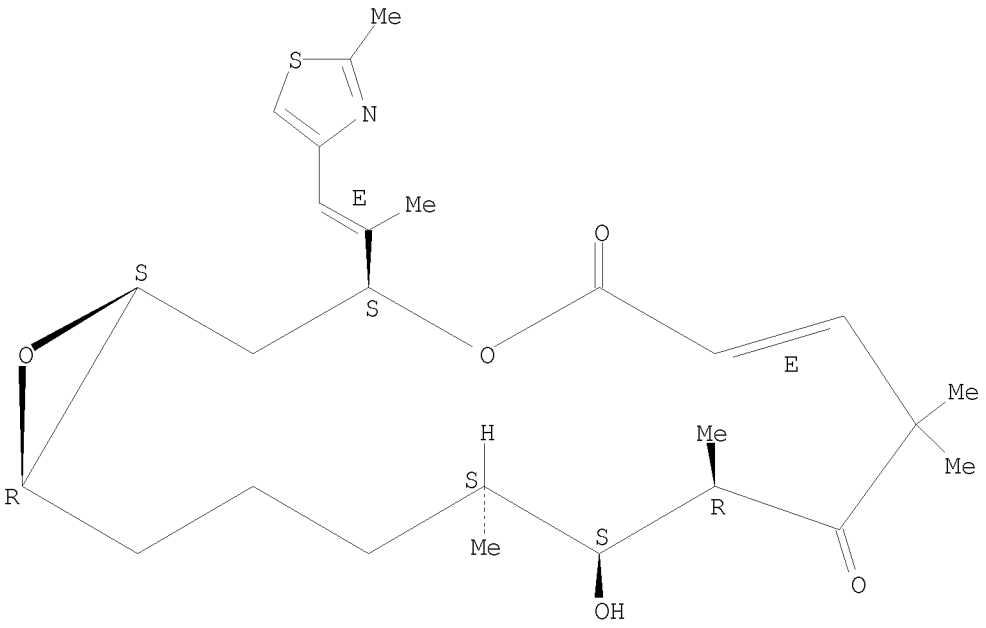
RN 226956-21-4 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 476623-83-3 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2002:655116 HCAPLUS
DOCUMENT NUMBER: 137:185358
TITLE: Preparation of epothilone analogs as anticancer agents
INVENTOR(S): Nicolaou, Kyriacos C.; He, Yun; Ninkovic, Sacha; Pastor, Joaquin; Roschangar, Frank; Sarabia, Francisco; Vallberg, Hans; Vourloumis, Dionisios; Winssinger, Nicolas; Yang, Zhen; King, N. Paul; Finlay, M. Ray
PATENT ASSIGNEE(S): The Scripps Research Institute, USA
SOURCE: U.S., 160 pp., Cont.-in-part of U. S. Ser. No. 856,533, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6441186	B1	20020827	US 1997-923869	19970904
CA 2274833	A1	19980618	CA 1997-2274833	19971212
WO 9825929	A1	19980618	WO 1997-EP7011	19971212

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,

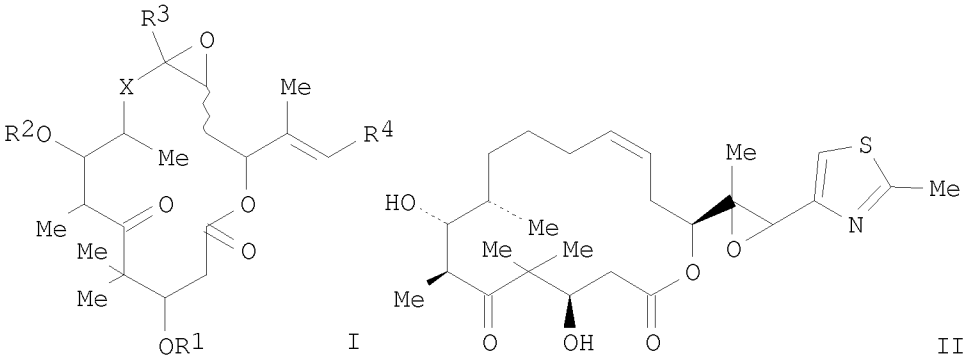
US, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9857577	A	19980703	AU 1998-57577	19971212
AU 746597	B2	20020502		
EP 944634	A1	19990929	EP 1997-953808	19971212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9714140	A	20000229	BR 1997-14140	19971212
CN 1246862	A	20000308	CN 1997-181771	19971212
CN 1134443	C	20040114		
JP 2001504856	T	20010410	JP 1998-526247	19971212
US 6380394	B1	20020430	US 1998-102602	19980622
US 20040127432	A1	20040701	US 2003-732698	20031209
US 7173137	B2	20070206		

PRIORITY APPLN. INFO.:

US 1996-32864P	P	19961213
US 1997-856533	B2	19970514
US 1997-923869	A	19970904
WO 1997-EP7011	W	19971212
US 1999-319885	A3	19990924

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 137:185358
GI



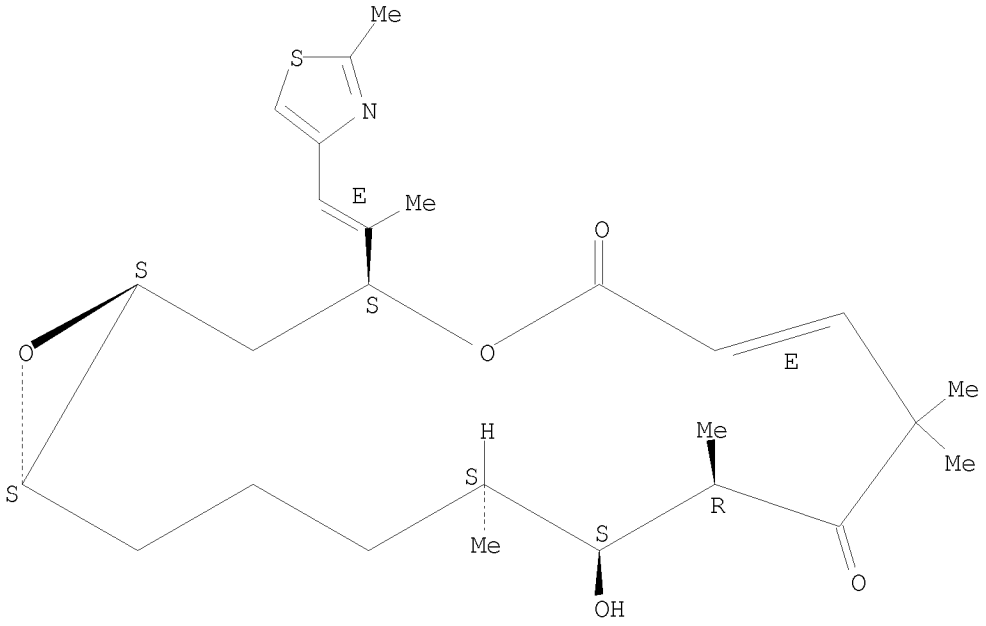
AB Epothilone A, epothilone B, analogs of epothilone and libraries of epothilone analogs of formula I [R1, R2 = H, silyl group, Me, Ac, PhCO, tert-butoxycarbonyl; R3 = H, Me, CHO, (substituted) CO2H, etc.; R4 = heterocyclyl, etc.; X = (CH2)n; n = 1-5] are synthesized. Epothilone A and B are known anticancer agents that derive their anticancer activity by the prevention of mitosis through the induction and stabilization of microtubulin assembly. Several of the analogs are demonstrated to have a superior cytotoxic activities as compared to epothilone A or epothilone B as demonstrated by their enhanced ability to induce the polymerization and stabilization of microtubules. Thus, epothilones A and B are prepared via olefin metathesis and macrocyclization. II was prepared and showed 7% tubulin polymerization

IT 193071-71-5P 193071-72-6P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(preparation of epothilone analogs as anticancer agents)

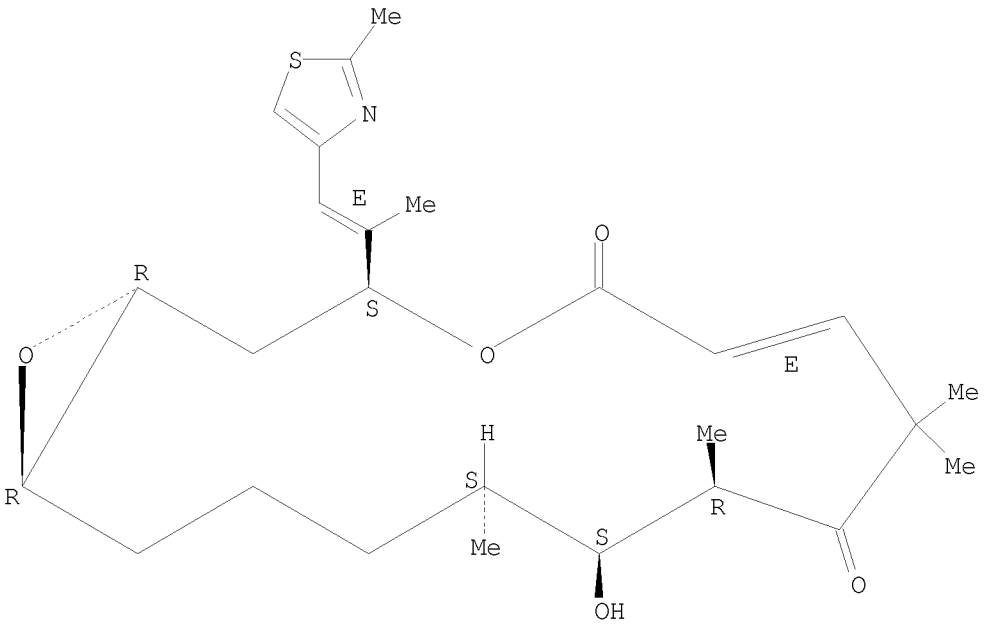
RN 193071-71-5 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193071-72-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:843887 HCAPLUS
DOCUMENT NUMBER: 135:371566
TITLE: Process for reduction of oxiranyl epothilones to olefinic epothilones
INVENTOR(S): Kim, Soong-hoon; Johnson, James A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 170,581. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6320045	B1	20011120	US 1999-316796	19990521
CA 2375029	A1	20001130	CA 2000-2375029	20000515
WO 2000071521	A1	20001130	WO 2000-US13253	20000515

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1178968	A1	20020213	EP 2000-930725		20000515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
HU 2002001467	A2	20021028	HU 2002-1467		20000515
HU 2002001467	A3	20050928			
JP 2003500394	T	20030107	JP 2000-619778		20000515
IN 2001MN01106	A	20070420	IN 2001-MN1106		20010912
MX 2001011053	A	20020722	MX 2001-11053		20011030
PRIORITY APPLN. INFO.:			US 1997-67549P	P	19971204
			US 1998-82563P	P	19980421
			US 1998-170581	A2	19981013
			US 1999-316796	A	19990521
			WO 2000-US13253	W	20000515

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 135:371566; MARPAT 135:371566
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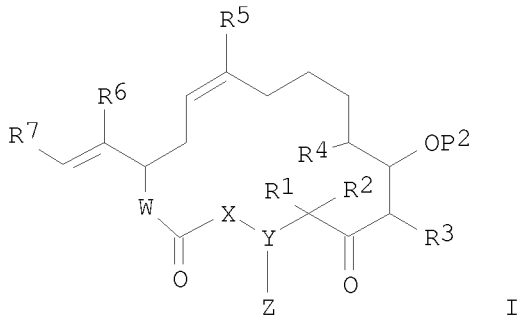

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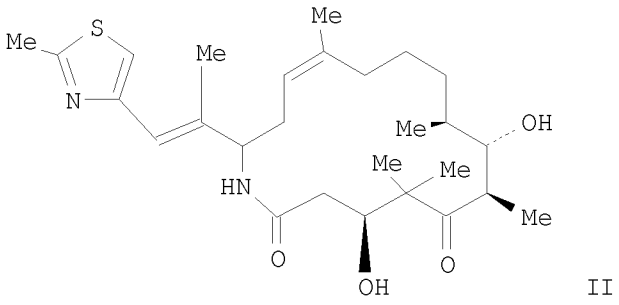


II

AB This process produced epothilones I (W = O, NR8; R1-R6 = H, (un)substituted alkyl or aryl and R1 and R2 can be cycloalkyl; R7 = H, (un)substituted alkyl, aryl, cycloalkyl or 4-7 membered heterocyclic N-, O-, or S-containing rings; R8 = H, (un)unsubstituted alkyl, OH, (un)unsubstituted O-alkyl; X = CH2 or XY = CH=CH; Z = H or OP1 where P1, P2 = H, (un)substituted alkyl, alkanoyl, aroyl, trialkyl(aryl)silyl) from oxiranyl epothilones via the reaction of the oxiranyl moiety with a metal or metal-assisted reagent selected from the group consisting of reactive metallocenes, or (WCl6, n-BuLi). Thus II was prepared in 29% yield in a

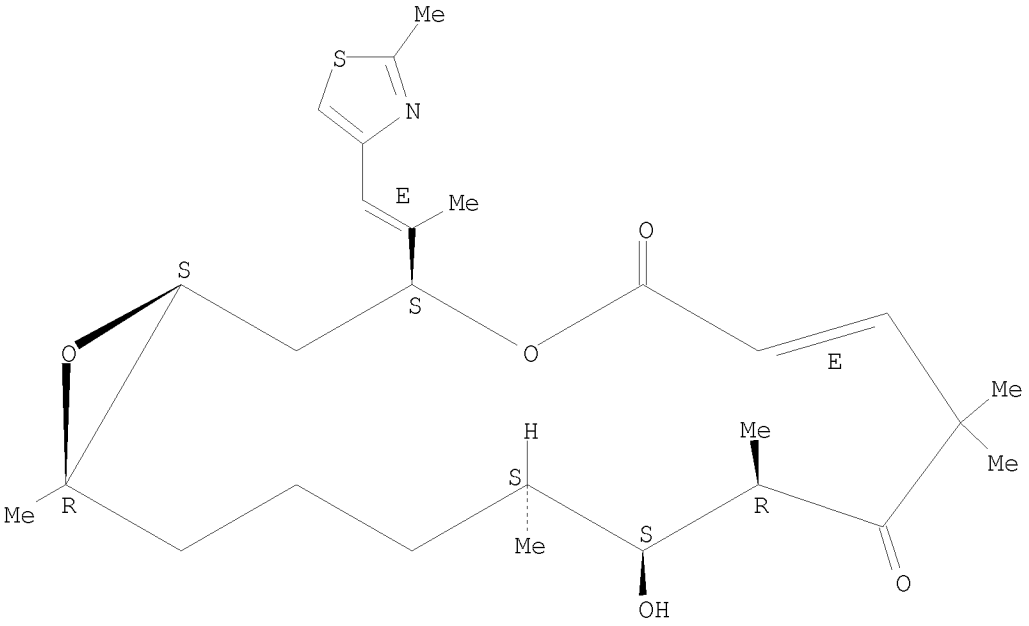
multistep reaction from epothilone B via the aminoheptadecenoic acid that cyclized to the oxiranyl azaepothilone intermediate which was reacted with WCl6 in THF and n-BuLi in hexane.

IT 226956-21-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for reduction of oxiranyl epothilones to olefinic epothilones)

RN 226956-21-4 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2001:137877 HCAPLUS
DOCUMENT NUMBER: 134:335980
TITLE: Comparative molecular field analysis (CoMFA) study of epothilones - tubulin depolymerization inhibitors: pharmacophore development using 3D QSAR methods
AUTHOR(S): Lee, Keun Woo; Briggs, James M.
CORPORATE SOURCE: Department of Biology and Biochemistry, University of Houston, Houston, TX, 77204-5513, USA
SOURCE: Journal of Computer-Aided Molecular Design (2001), 15(1), 41-55
CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal

LANGUAGE: English

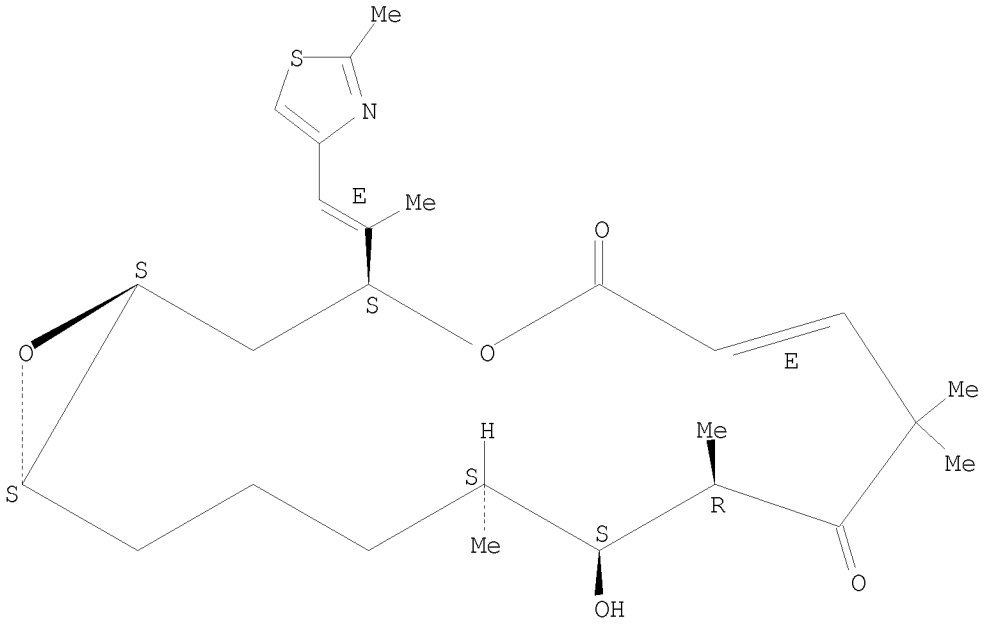
AB A three-dimensional quant. structure-activity relationship (3D QSAR) study has been carried out on epothilones based on comparative mol. field analyses (CoMFA) using a large data set of epothilone analogs, which are potent inhibitors of tubulin depolymn. Microtubules, which are polymers of the α/β-tubulin heterodimer, need to dissociate in order to form the mitotic spindle, a structure required for cell division. A rational pharmacophore searching method using 3D QSAR procedures was carried out and the results for the epothilones are described herein. One-hundred and sixty-six epothilone analogs and their depolymn. inhibition properties with tubulin were used as a training set. Over a thousand mol. field energies were generated and applied to generate the descriptors of QSAR equations. Using a genetic function algorithm (GFA) method, combined with a least square approach, multiple QSAR models were considered during the search for pharmacophore elements. Each GFA run resulted in 100 QSAR models, which were ranked according to their lack of fit (LOF) scores, with a total of 40 GFA runs having been performed. The 40 best QSAR equations from each run had adequate fitted correlation coeffs. (R from 0.813 to 0.863) and were of sufficient statistical significance (F value from 7.2 to 10.9). The pharmacophore elements for epothilones were studied by investigating the hit frequency of descriptors (i.e. the sampling probabilities of grid points from the GFA studies) from the set of the 4000 top scoring QSAR equations. By comparing the frequency with which each grid point appeared in the QSAR equations, three candidate regions in the epothilones were proposed to be pharmacophore elements. Two of them are completely compatible with the recent model proposed by Ojima et al. however, one is quite different and is necessary to accurately predict the activities of all 166 epothilone mols. used in our training set. Finally, by visualizing the 35 most probable grid points, it was found that changes related to the C6, C7, C8, C12, S20, and C21 atoms of the epothilones were highly correlated to their activity.

IT 193071-71-5 193071-72-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(CoMFA study of epothilones - tubulin depolymn. inhibitors: pharmacophore development using 3D QSAR methods)

RN 193071-71-5 HCAPLUS

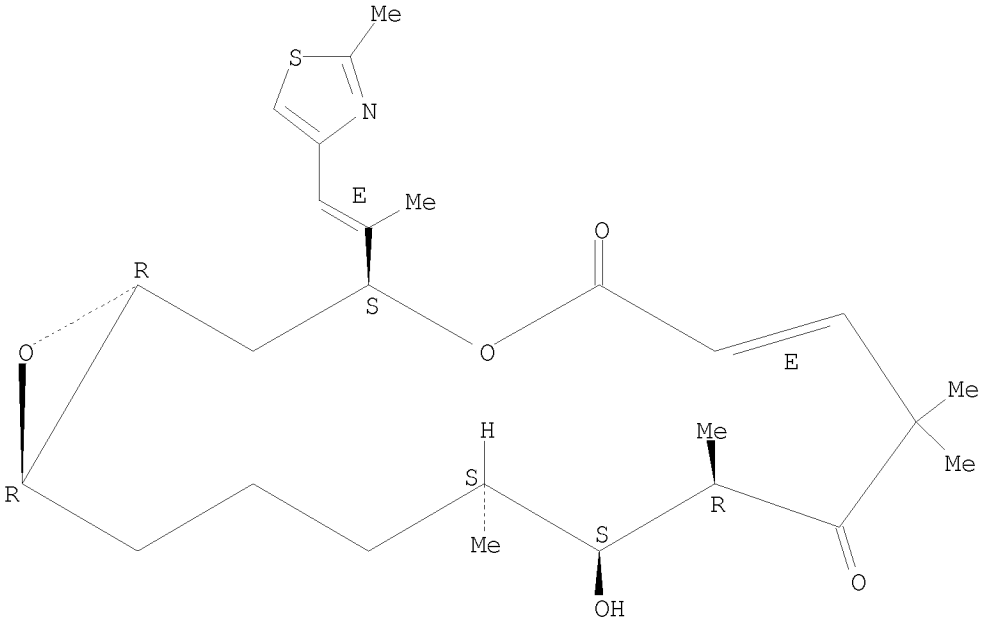
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193071-72-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



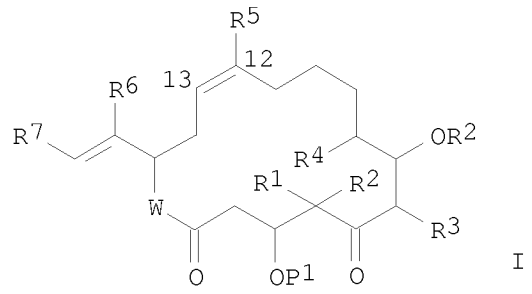
OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2000:842116 HCAPLUS
DOCUMENT NUMBER: 133:362657
TITLE: A process for the reduction of oxiranyl epothilones to olefinic epothilones
INVENTOR(S): Kim, Soong-Hoon; Johnson, James A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

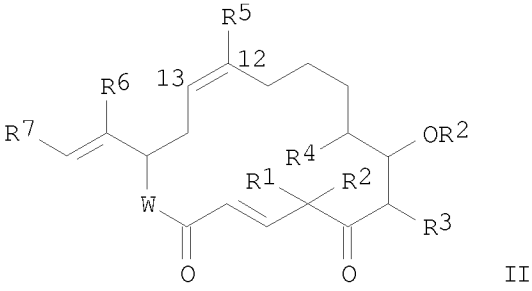
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071521	A1	20001130	WO 2000-US13253	20000515
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6320045	B1	20011120	US 1999-316796	19990521
CA 2375029	A1	20001130	CA 2000-2375029	20000515
EP 1178968	A1	20020213	EP 2000-930725	20000515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500394	T	20030107	JP 2000-619778	20000515
IN 2001MN01106	A	20070420	IN 2001-MN1106	20010912
MX 2001011053	A	20020722	MX 2001-11053	20011030

PRIORITY APPLN. INFO.:	US 1999-316796	A	19990521
	US 1997-67549P	P	19971204
	US 1998-82563P	P	19980421
	US 1998-170581	A2	19981013
	WO 2000-US13253	W	20000515

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 133:362657; MARPAT 133:362657
GI



I



II

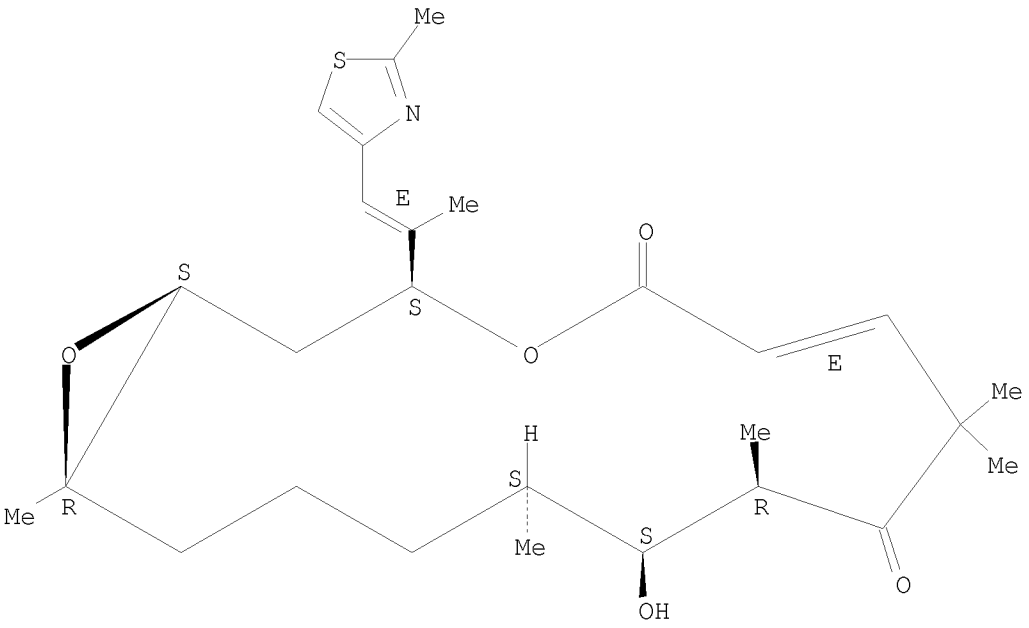
AB 12(13)-Olefinic epothilones, such as I and II [R1-6 = H, alkyl, aryl; R1R2 = cycloalkyl; R7 = H, alkyl, aryl, cycloalkyl, heterocyclyl; P1, P2 = H, alkyl, alkanoyl, aroyl, silyl, etc.; W = O, NR8; R8 = H, OH, alkyl], were prepared via reduction of the corresponding 12,13-epoxyepothilones using a metal or metal-assisted reagent. The metal or metal-assisted reagent was selected from the group consisting of reactive metallocenes, [N2C(CO2Me)2, cat Rh2(OAc)4], [N2C(CO2Me)2, cat[(n-C7H15CO2)2Rh]2], [Zn-Cu, EtOH], [Mg(Hg), MgBr], Cr, [FeCl3, n-BuLi], [TiCl3, LiAlH4], [TiCl4, Zn], [WCl6, LiAlH4], [NbCl5, NaAlH4], [VCl3,Zn], or [WCl6, n-BuLi]. Thus, epothilone A, a 12,13-epoxyepothilone, was reduced using magnesium turnings and titanocene dichloride in THF to give epothilone C, a 12(13)-(Z)-olefin, in 80% yield.

IT 226956-21-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the reduction of oxiranyl epothilones to olefinic epothilones)

RN 226956-21-4 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2000:316343 HCAPLUS
Correction of: 1997:528752
DOCUMENT NUMBER: 132:293587
Correction of: 127:149021
TITLE: The Olefin Metathesis Approach to Epothilone A and Its Analogs
AUTHOR(S): Nicolaou, K. C.; He, Y.; Vourloumis, D.; Vallberg, H.; Roschangar, F.; Sarabia, F.; Ninkovic, S.; Yang, Z.; Trujillo, J. I.
CORPORATE SOURCE: Institute for Chemical Biology, La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (1997), 119(34), 7960-7973
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

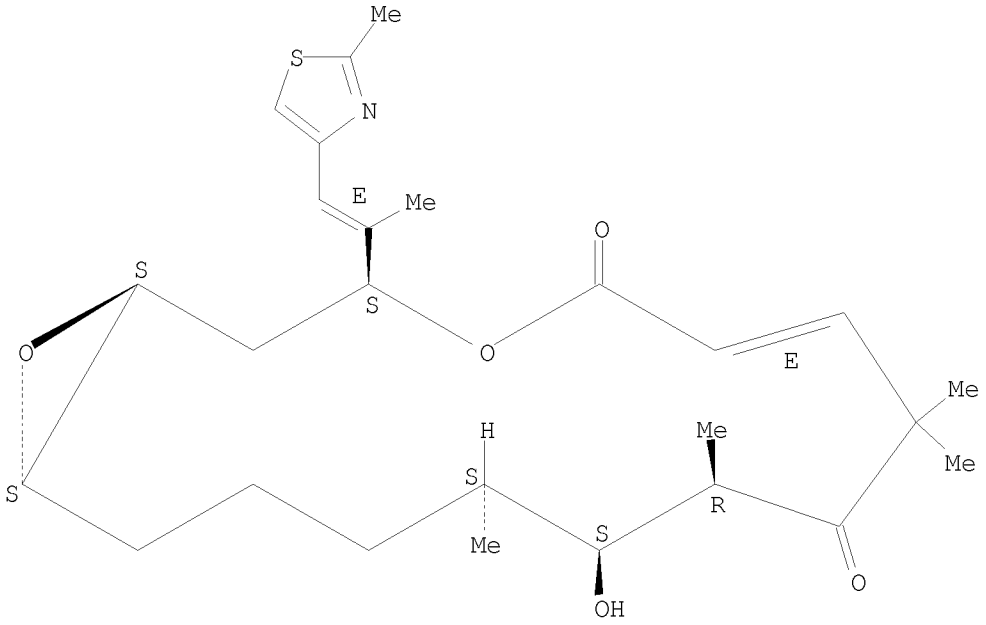
AB The olefin metathesis approach to epothilone A (I) and several diastereomeric analogs is described. Key building blocks II,

(S)-OHCCH(Me)CH2CH2CH2CH=CH2, and (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H were constructed in optically active form and were coupled and elaborated to olefin metathesis precursor III (R = SiMe2CMe3) via an aldol reaction and an esterification coupling. Olefin metathesis of compound III (R = SiMe2CMe3), under the catalytic influence of RuCl2(:CHPh)(PCy3)2, furnished cis- and trans-cyclic olefins IV (R = SiMe2CMe3). Epoxidn. of (Z)-IV (R = H) gave I and several analogs, whereas epoxidn. of (E)-IV (R = H) resulted in addnl. epothilones. Similar elaboration of isomeric as well as simpler intermediates resulted in yet another series of epothilone analogs and model systems.

IT 193071-71-5P 193071-72-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of epothilone A and analogs via olefin metathesis)

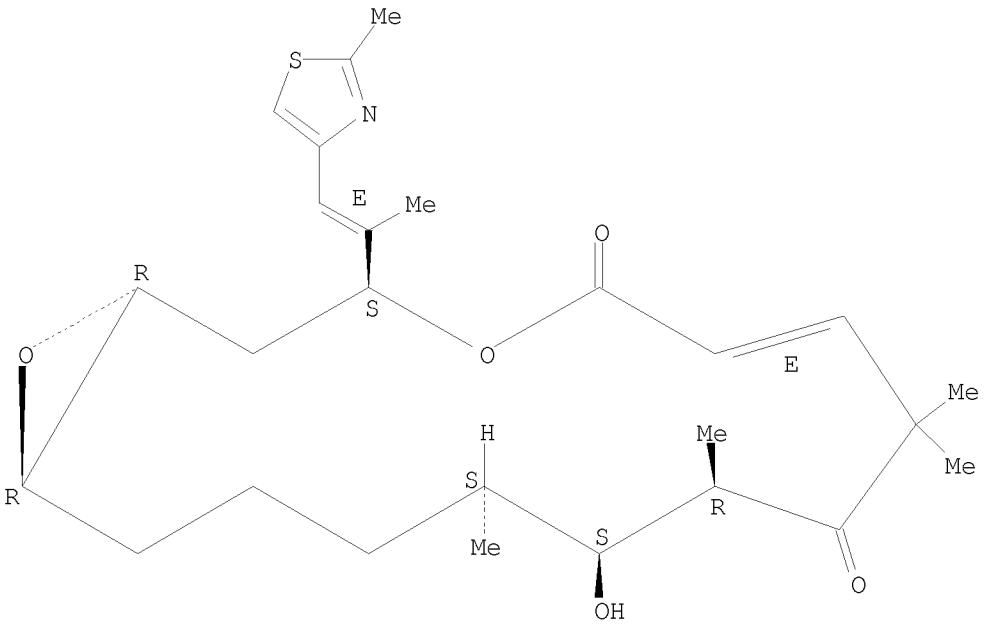
RN 193071-71-5 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193071-72-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



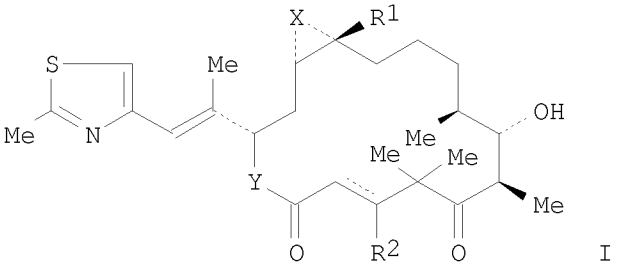
L7 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1999:691091 HCAPLUS
DOCUMENT NUMBER: 131:310502
TITLE: synthesis and cytotoxicity of 12,13-modified epothilone derivatives for use in treatment of tumors or other hyperproliferative cellular disease
INVENTOR(S): Vite, Gregory D.; Kim, Soong-Hoon Kim; Hofle, Gerhard
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954319	A1	19991028	WO 1999-US7475	19990405
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG				
US 6380395	B1	20020430	US 1999-280192	19990329
US 6399638	B1	20020604	US 1999-280191	19990329
CA 2329181	A1	19991028	CA 1999-2329181	19990405
AU 9934716	A	19991108	AU 1999-34716	19990405
AU 748526	B2	20020606		
BR 9909795	A	20001226	BR 1999-9795	19990405

TR 2000003036	T2	20010122	TR 2000-3036	19990405
EP 1073648	A1	20010207	EP 1999-916383	19990405
EP 1073648	B1	20060920		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
JP 2002512239	T	20020423	JP 2000-544658	19990405
CN 1142923	C	20040324	CN 1999-805266	19990405
EP 1589017	A2	20051026	EP 2005-15236	19990405
EP 1589017	A3	20090422		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 340177	T	20061015	AT 1999-916383	19990405
PT 1073648	E	20061229	PT 1999-916383	19990405
ES 2273484	T3	20070501	ES 1999-916383	19990405
PT 1073647	E	20090717	PT 1999-915273	19990405
ES 2327803	T3	20091103	ES 1999-915273	19990405
MX 2000010109	A	20010419	MX 2000-10109	20001016

PRIORITY APPLN. INFO.:	US 1998-82564P	P	19980421
	EP 1999-916383	A3	19990405
	WO 1999-US7475	W	19990405

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 131:310502
GI



I

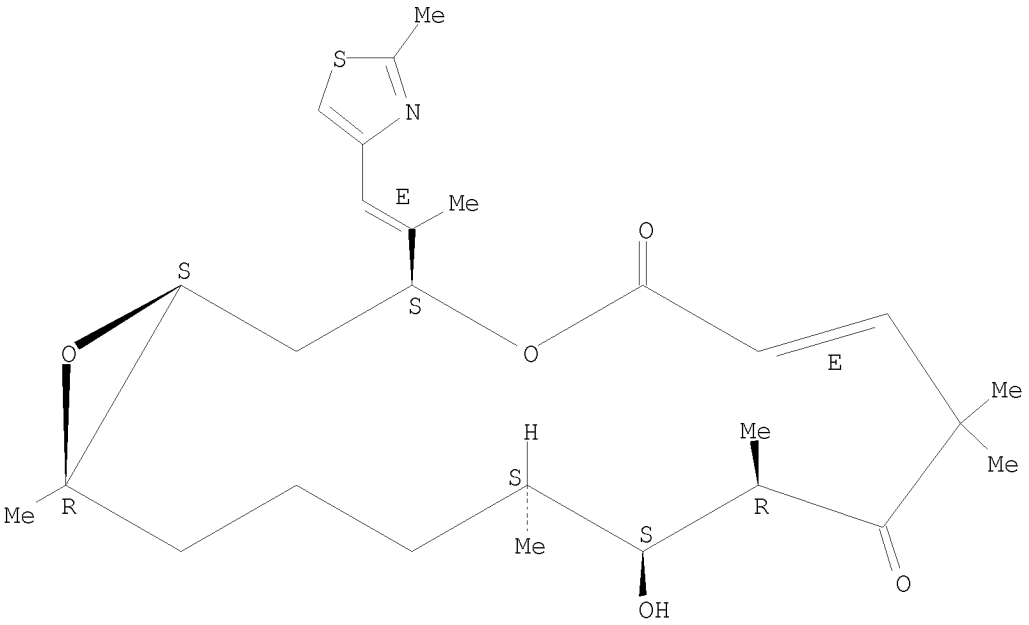
AB Synthesis and cytotoxicity of 12,13-modified epothilone derivs.(I) [R1 = H, (un)substituted alkyl; R2 = H if bond double or βOH if bond single; Y = O, NH; X = O, (un)substituted NH, OCH2, 2-methylthiazolo, S, (un)substituted CH2] is presented. Thus, I (R1 = H, X = NH, R2 = βOH, Y = O) (II) is prepared by epoxidn. of epothilone C followed by azidation and reductive imination. I are useful in treatment of tumors or other hyperproliferative cellular disease and show IC50 of 0.01-1000 nM in cell proliferation tests.

IT 226956-21-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxicity of 12,13-modified epothilone derivs. for use in treatment of tumors or other hyperproliferative cellular disease)

RN 226956-21-4 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1999:375551 HCAPLUS
DOCUMENT NUMBER: 131:31830
TITLE: A process for the reduction of oxiranyl epothilones to olefinic epothilones
INVENTOR(S): Kim, Soong-Hoon; Johnson, James A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

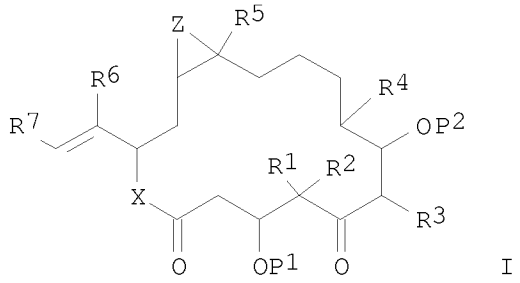
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928324	A1	19990610	WO 1998-US25464	19981201

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

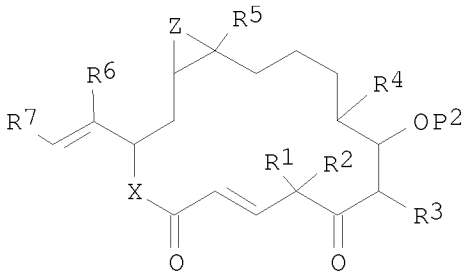
	CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2311929		A1	19990610	CA 1998-2311929	19981201
AU 9915408		A	19990616	AU 1999-15408	19981201
AU 738576		B2	20010920		
EP 1042327		A1	20001011	EP 1998-959652	19981201
EP 1042327		B1	20030917		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
HU 2001000582		A2	20010928	HU 2001-582	19981201
HU 2001000582		A3	20030328		
JP 2001525324		T	20011211	JP 2000-523216	19981201
JP 4434484		B2	20100317		
IL 135590		A	20030917	IL 1998-135590	19981201
AT 250066		T	20031015	AT 1998-959652	19981201
ES 2207015		T3	20040516	ES 1998-959652	19981201
TW 221469		B	20041001	TW 1998-87119880	19981201
HK 1028401		A1	20040514	HK 2000-107869	20001207
PRIORITY APPLN. INFO.:				US 1997-67549P P	19971204
				US 1998-82563P P	19980421
				WO 1998-US25464 W	19981201

OTHER SOURCE(S): CASREACT 131:31830; MARPAT 131:31830

GI



I



II

AB The olefinic epothilones I and II (X = O, NR8; Z = bond; R1-R6 = H, alkyl, substituted alkyl, aryl; R1R2 may be a cycloalkyl; R7 = H, alkyl, substituted alkyl, aryl, cycloalkyl, heterocyclo; R8 = H, alkyl, substituted alkyl, OH, alkoxy, substituted alkoxy; P1, P2 = H, alkyl, substituted alkyl, alkanoyl, substituted alkanoyl, aroyl, substituted aroyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl) were prepared by reduction of the oxiranyl epothilones I and II (Z = O) with a

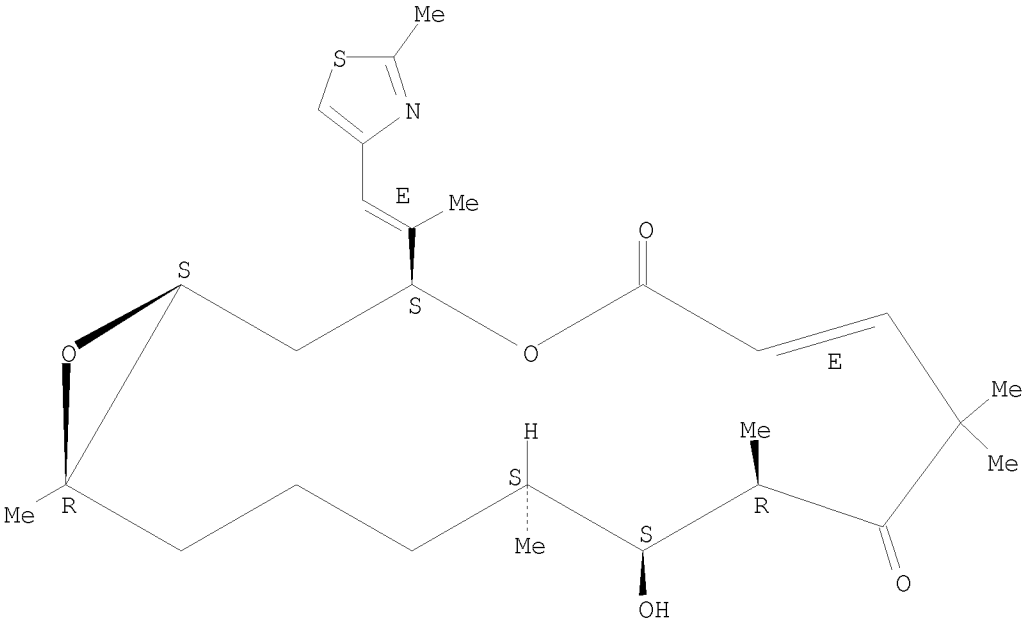
metal or metal assisted reagents, e.g. metallocenes, WCl4-BuLi, VCl3-Zn, TiCl3-LiAlH4. Thus, epothilone A was treated with Mg and bis(cyclopentadienyl)titanium dichloride in THF to give 80% epothilone C.

IT 226956-21-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for reduction of oxiranyl epothilones to olefinic epothilones)

RN 226956-21-4 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

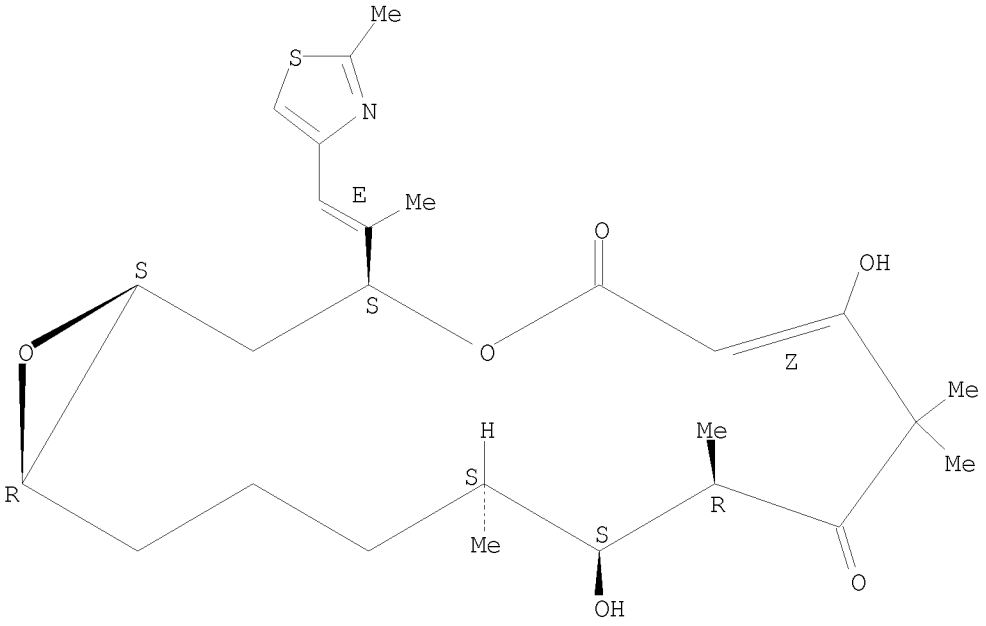


OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:760825 HCAPLUS
DOCUMENT NUMBER: 130:95406
TITLE: Oxidative and reductive transformations of epothilone A
AUTHOR(S): Sefkow, Michael; Kiffe, Michael; Schummer, Dietmar; Hofle, Gerhard
CORPORATE SOURCE: Gesellschaft fur Biotechnologische Forschung mbH, Abt, Naturstoffchemie, Braunschweig, D-38124, Germany
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(21), 3025-3030
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:95406
AB The C7 hydroxy group of cytotoxic epothilone A was selectively oxidized using PDC. A selective oxidation of the C3 hydroxy group was accomplished with Me2S/(PhCO2)2 after in situ protection of C7-OH. Reduction of epothilone A or of a C5, C7 dioxo derivative with NaBH4 proceeded at the C5 carbonyl group. Oxidation and hydrogenation of the C16-C17 double bond proved to be difficult but it was easily cleaved with ozone and the resulting keto derivative was transformed to epothilone analogs with different side chains.
IT 219557-03-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(oxidative and reductive transformations of epothilone A)
RN 219557-03-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6Z,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

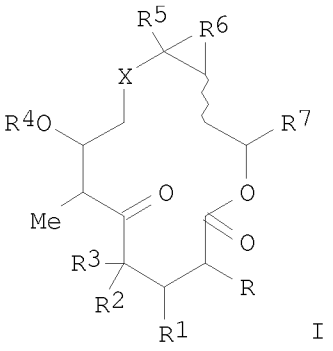
L7 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1998:405952 HCAPLUS
DOCUMENT NUMBER: 129:81625
ORIGINAL REFERENCE NO.: 129:16853a,16856a
TITLE: Preparation of epothilone analogs as anticancer agents
INVENTOR(S): Nicolaou, Costa Kyriacos; He, Yun; Ninkovic, Sacha;

Pastor, Joaquin; Roschangar, Frank; Sarabia, Francisco; Vallberg, Hans; Vourloumis, Dionisios; Winssinger, Nicolas; Yang, Zhen; King, Nigel Paul; et al.
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Scripps Research Institute
SOURCE: PCT Int. Appl., 213 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9825929	A1	19980618	WO 1997-EP7011	19971212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6441186	B1	20020827	US 1997-923869	19970904
CA 2274833	A1	19980618	CA 1997-2274833	19971212
AU 9857577	A	19980703	AU 1998-57577	19971212
AU 746597	B2	20020502		
EP 944634	A1	19990929	EP 1997-953808	19971212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9714140	A	20000229	BR 1997-14140	19971212
JP 2001504856	T	20010410	JP 1998-526247	19971212
US 6660758	B1	20031209	US 1999-319885	19990924
US 20040127432	A1	20040701	US 2003-732698	20031209
US 7173137	B2	20070206		

PRIORITY APPLN. INFO.:	US 1996-32864P	P	19961213
	US 1997-856533	A	19970514
	US 1997-923869	A2	19970904
	WO 1997-EP7011	W	19971212
	US 1999-319885	A3	19990924

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 129:81625
GI



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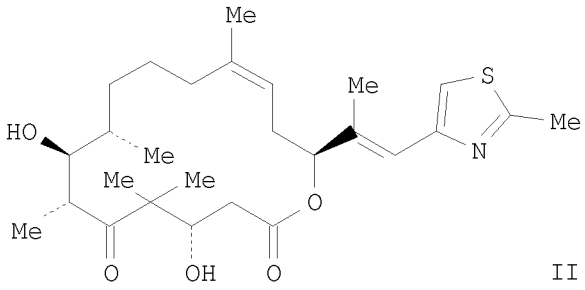


II

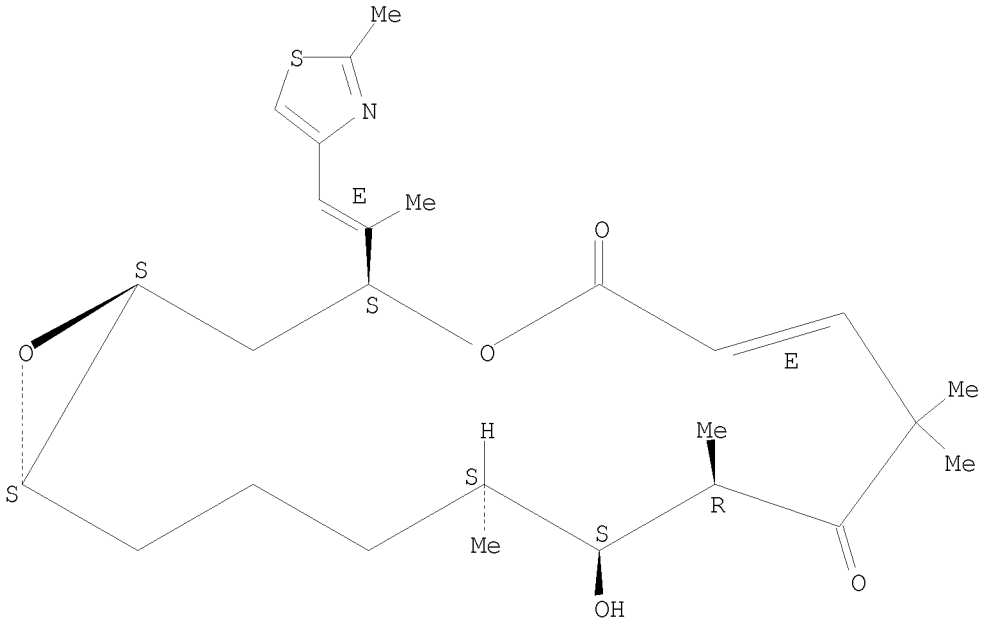
AB Epothilone A, epothilone B, analogs of epothilone and libraries of epothilone analogs of formula I [X = (CH2)n; n = 1-5; R1 = OH, OMe, absent; R2, R3 = H, CH2, Me; R4 = H, Me, protecting group; R5 = H, Me, CHO, (substituted) CO2H, etc.; R6 = O, CH2, absent; R7 = thiazolealkyl, etc.] are synthesized. Epothilone A and B are known anticancer agents that derive their anticancer activity by the prevention of mitosis through the induction and stabilization of microtubulin assembly. Several of the analogs are demonstrated to have a superior cytotoxic activity as compared to epothilone A or epothilone B as demonstrated by their enhanced ability to induce the polymerization and stabilization of microtubules. Thus, II was prepared and was shown to induce tubulin polymerization at 94% relative to GTP, and inhibit carcinoma cell growth.

IT 193071-71-5P 193071-72-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone analogs as anticancer agents)

RN 193071-71-5 HCAPLUS

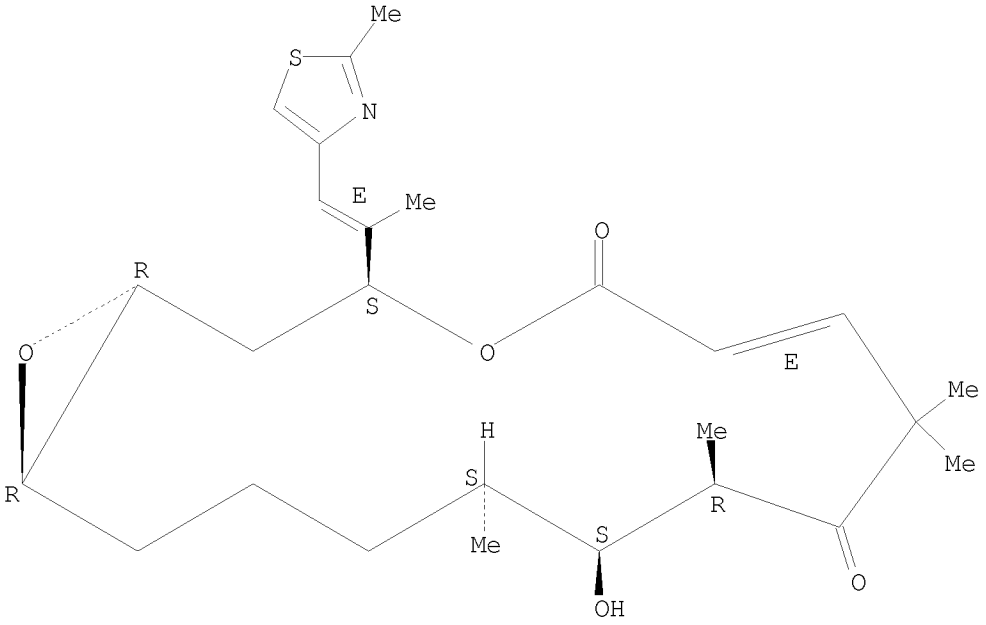
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193071-72-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

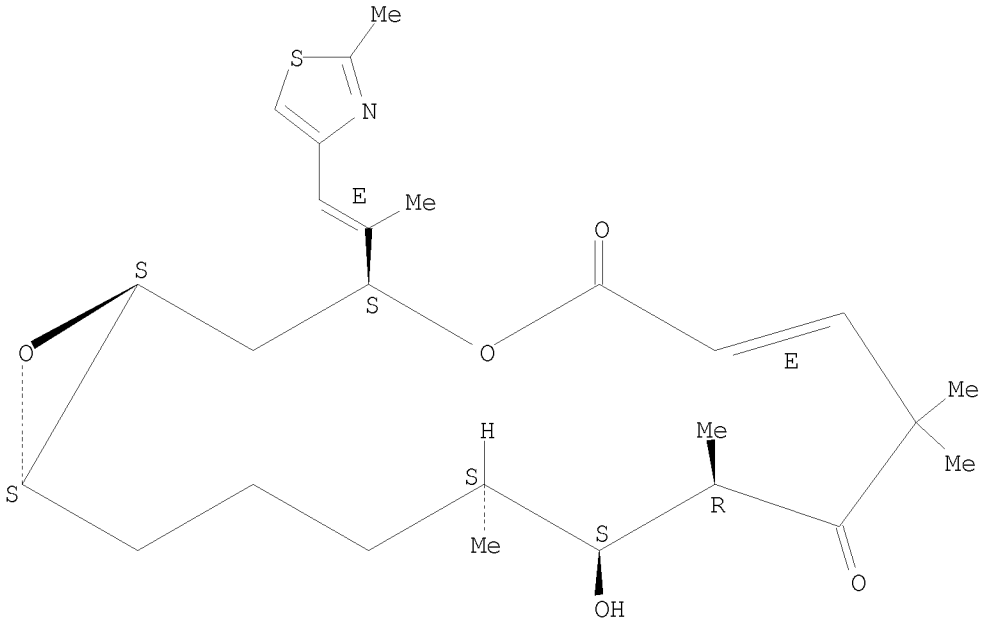
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



OS.CITING REF COUNT: 28 THERE ARE 28 CAPLUS RECORDS THAT CITE THIS RECORD (28 CITINGS)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

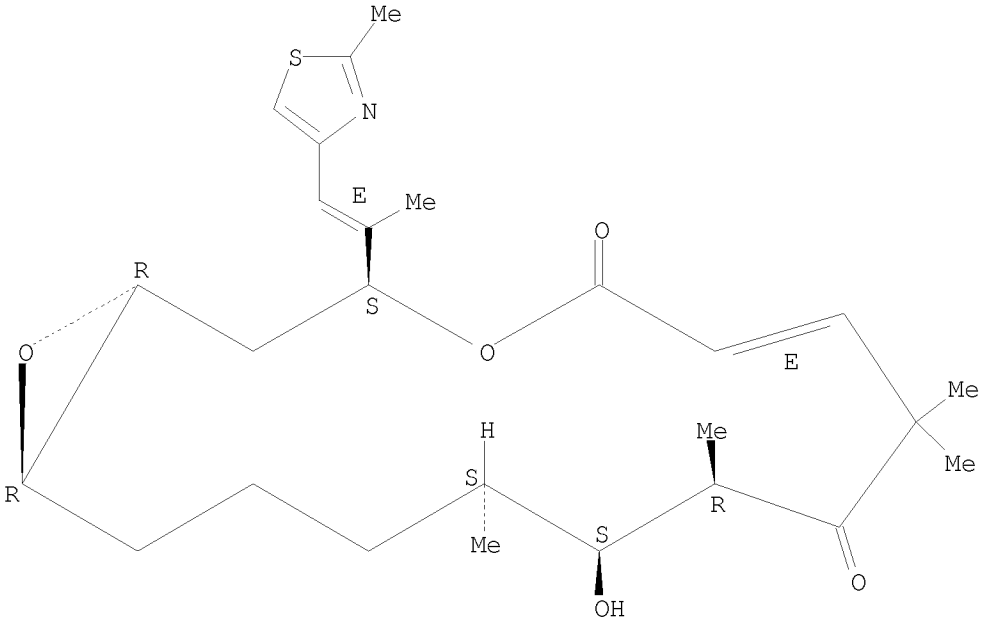
L7 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:714315 HCAPLUS
DOCUMENT NUMBER: 128:3560
ORIGINAL REFERENCE NO.: 128:771a
TITLE: Designed epothilones: combinatorial synthesis, tubulin assembly properties, and cytotoxic action against taxol-resistant tumor cells
AUTHOR(S): Nicolaou, K. C.; Vourloumis, Dionisios; Li, Tianhu; Pastor, Joaquin; Winssinger, Nicolas; He, Yun; Ninkovic, Sacha; Sarabia, Francisco; Vallberg, Hans; Roschangar, Frank; King, N. Paul; Finlay, M. Ray V.; Giannakakou, Pareskevi; Verdier-Pinard, Pascal; Hamel, Ernest
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(19), 2097-2103
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title work demonstrates the power of interfacing combinatorial chemical with chemical biol. as facilitated by solid-phase synthesis, radiofrequency encoded combinatorial chemical and modern biol. assays. A library of 112 epothilones were prepared by solid-phase synthesis, their structure activity relationships measured by tubulin binding assay and some tested for inhibition of carcinoma cell growth.
IT 193071-71-5P 193071-72-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combinatorial synthesis of epothilone library, tubulin assembly properties, and cytotoxic action against taxol-resistant tumor cells)
RN 193071-71-5 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193071-72-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

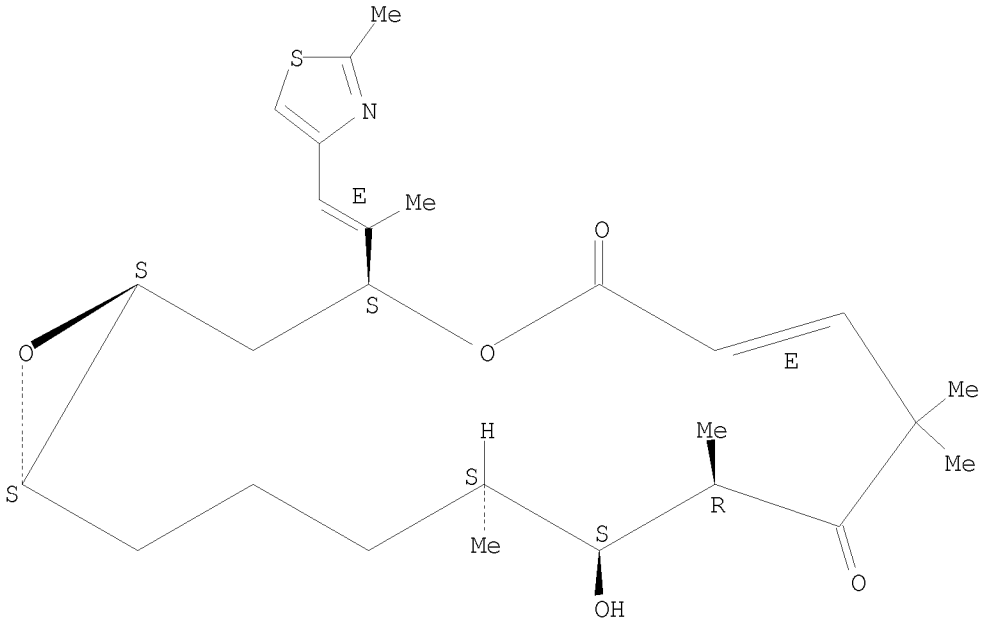
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



OS.CITING REF COUNT: 200 THERE ARE 200 CAPLUS RECORDS THAT CITE THIS RECORD (204 CITINGS)
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

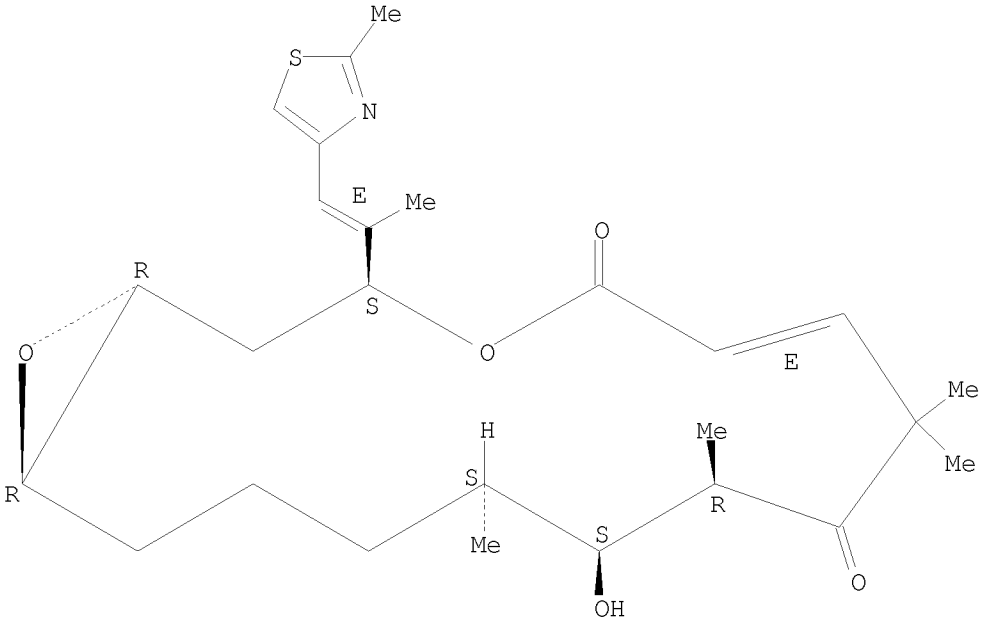
L7 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:528752 HCAPLUS
DOCUMENT NUMBER: 127:149021
ORIGINAL REFERENCE NO.: 127:28789a,28792a
TITLE: The Olefin Metathesis Approach to Epothilone A and Its Analogs
AUTHOR(S): Nicolaou, K. C.; He, Y.; Vourloumis, D.; Vallberg, H.; Roschangar, F.; Sarabia, F.; S.Ninkovic; Yang, Z.; Trujillo, J. I.
CORPORATE SOURCE: Department of Chemistry and The Skaggs, Institute for Chemical Biology, La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (1997), 119(34), 7960-7973
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:149021
GI For diagram(s), see printed CA Issue.
AB The olefin metathesis approach to epothilone A (I) and several diastereomeric analogs is described. Key building blocks II, (S)-OHCCH(Me)CH2CH2CH2CH=CH2, and (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H were constructed in optically active form and were coupled and elaborated to olefin metathesis precursor III (R = SiMe2CMe3) via an aldol reaction and an esterification coupling. Olefin metathesis of compound III (R = SiMe2CMe3), under the catalytic influence of RuCl2(:CHPh)(PCy3)2, furnished cis- and trans-cyclic olefins IV (R = SiMe2CMe3). Epoxidn. of (Z)-IV (R = H) gave I and several analogs, whereas epoxidn. of (E)-IV (R = H) resulted in addnl. epothilones. Similar elaboration of isomeric as well as simpler intermediates resulted in yet another series of epothilone analogs and model systems.
IT 193071-71-5P 193071-72-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of epothilone A and analogs via olefin metathesis)
RN 193071-71-5 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193071-72-6 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

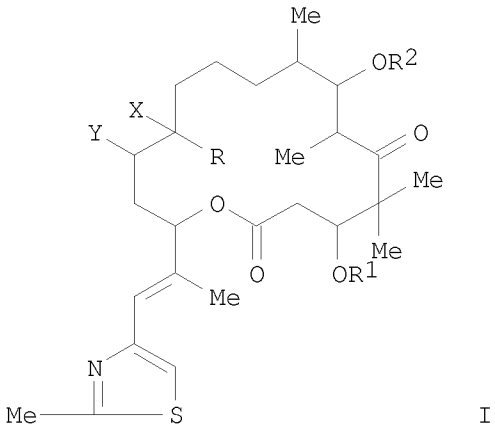


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L7 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:456769 HCAPLUS
DOCUMENT NUMBER: 127:50474
ORIGINAL REFERENCE NO.: 127:9629a
TITLE: Preparation of epothilone derivatives as agrochemicals and pharmaceuticals
INVENTOR(S): Hoefle, Gerhard; Kiffe, Michael
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung Mbh (Gbf), Germany
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19542986	A1	19970522	DE 1995-19542986	19951117
WO 9719086	A1	19970529	WO 1996-EP5080	19961118
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 873341	A1	19981028	EP 1996-939097	19961118
EP 873341	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 903348	A1	19990324	EP 1998-121523	19961118
EP 903348	B1	20020605		
EP 903348	B2	20080827		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000500757	T	20000125	JP 1997-519381	19961118
JP 4183099	B2	20081119		
EP 1186606	A1	20020313	EP 2001-127352	19961118
EP 1186606	B1	20040317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 218556	T	20020615	AT 1998-121523	19961118
PT 903348	E	20021129	PT 1998-121523	19961118
ES 2178093	T3	20021216	ES 1998-121523	19961118
AT 249463	T	20030915	AT 1996-939097	19961118
PT 873341	E	20040227	PT 1996-939097	19961118
AT 261961	T	20040415	AT 2001-127352	19961118
ES 2206607	T3	20040516	ES 1996-939097	19961118
EP 1440973	A2	20040728	EP 2004-5011	19961118
EP 1440973	A3	20041020		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PT 1186606	E	20040831	PT 2001-127352	19961118
ES 2218328	T3	20041116	ES 2001-127352	19961118
US 6288237	B1	20010911	US 1998-77055	19980803
US 20010034452	A1	20011025	US 2001-836134	20010416
US 6613912	B2	20030902		
US 20040087634	A1	20040506	US 2003-602770	20030625

US 6831076 B2 20041214
PRIORITY APPLN. INFO.: DE 1995-19542986 A 19951117
DE 1996-19639456 A 19960925
EP 1996-939097 A3 19961118
EP 2001-127352 A3 19961118
WO 1996-EP5080 W 19961118
US 1998-77055 A3 19980803
US 2001-836134 A3 20010416
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 127:50474
GI



I

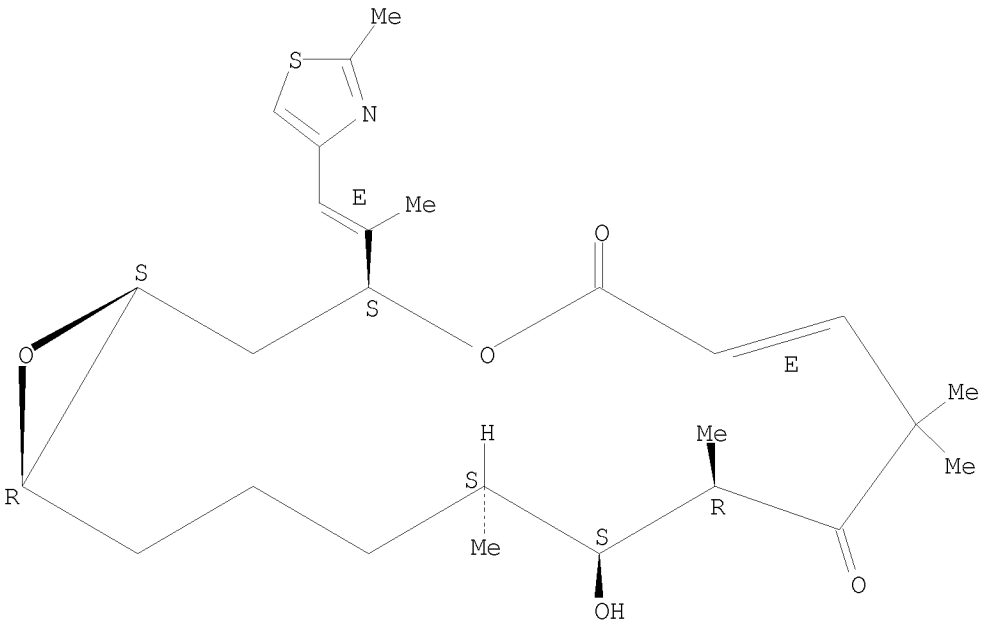
AB The title compds., e.g., I [R = H, C1-4 alkyl; R1, R2 = H, C1-6 alkyl, C1-6 acyl, benzoyl, C1-4 trialkylsilyl, benzyl, Ph, C1-6 alkoxy, C6 alkyl-, hydroxy-, and halo-substituted benzyl or phenyl; X, Y = halo, OH, acyloxy, alkoxy, benzoyloxy] , useful as agrochems. and pharmaceuticals (no data), are prepared Thus, epothilone A in acetone containing trifluoroacetic acid was heated overnight at 50° and the reaction mixture was adjusted to pH 7 with 1 M phosphate buffer to give 2 isomers, each in 19% yield.

IT 191105-88-1P
RL: AGR (Agricultural use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone derivs. as agrochems. and pharmaceuticals)

RN 191105-88-1 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),6E,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



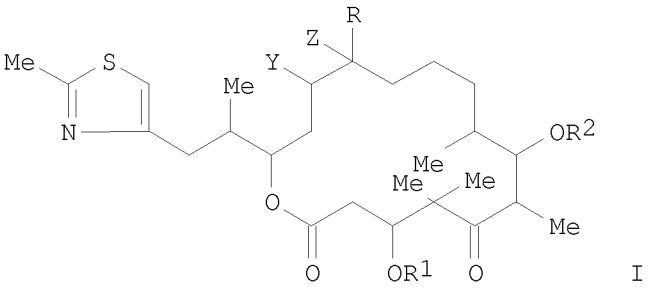
OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

L7 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 1997:443365 HCAPLUS
DOCUMENT NUMBER: 127:81289
ORIGINAL REFERENCE NO.: 127:15585a,15588a
TITLE: Preparation of epothilone derivatives as agrochemicals and pharmaceuticals
INVENTOR(S): Hofle, Gerhard; Kiffe, Michael
PATENT ASSIGNEE(S): Gesellschaft Fur Biotechnologische Forschung Mbh (Gbf), Germany; Hofle, Gerhard; Kiffe, Michael
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719086	A1	19970529	WO 1996-EP5080	19961118
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19542986	A1	19970522	DE 1995-19542986	19951117
DE 19639456	A1	19980326	DE 1996-19639456	19960925
EP 873341	A1	19981028	EP 1996-939097	19961118
EP 873341	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000500757	T	20000125	JP 1997-519381	19961118
JP 4183099	B2	20081119		

AT 249463	T	20030915	AT 1996-939097		19961118
US 6288237	B1	20010911	US 1998-77055		19980803
US 20040087634	A1	20040506	US 2003-602770		20030625
US 6831076	B2	20041214			
PRIORITY APPLN. INFO.:			DE 1995-19542986	A	19951117
			DE 1996-19639456	A	19960925
			WO 1996-EP5080	W	19961118
			US 1998-77055	A3	19980803
			US 2001-836134	A3	20010416

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 127:81289
GI



I

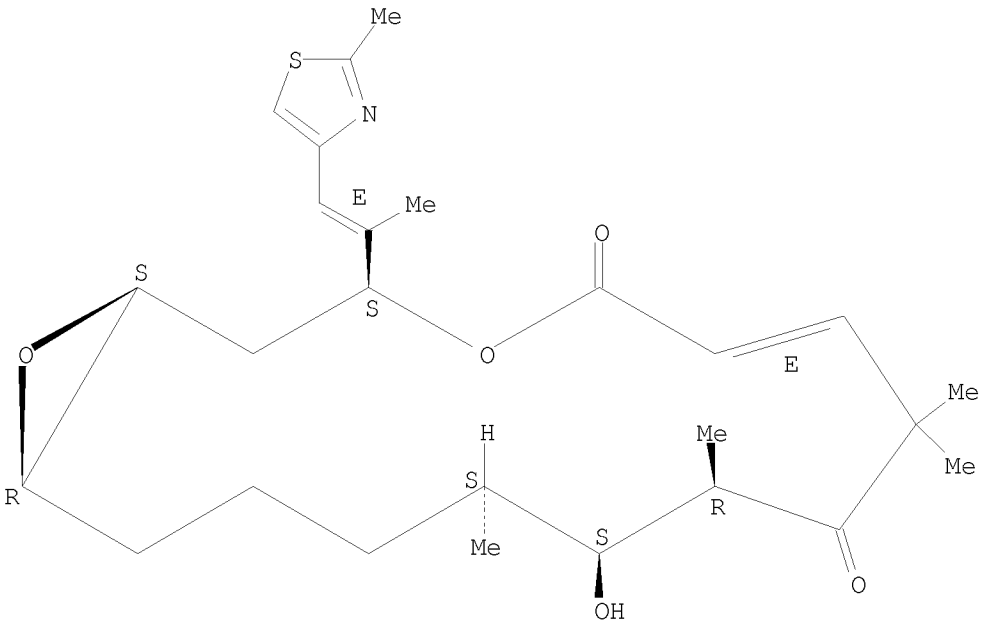
AB The title compds., e.g., I [R = H, C1-4 alkyl; R1, R2 = H, C1-6 alkyl, C1-6 acyl, benzoyl, C1-4 trialkylsilyl, benzyl, Ph, C1-6 alkoxy, C6 alkyl-, hydroxy-, and halo-substituted benzyl or phenyl; X, Y = H, halo, pseudohalo, OH, acyloxy, alkoxy, benzoyloxy; or YZ = O, bond; however, I may not be epothilone A or B] , useful as agrochems. and pharmaceuticals (no data), are prepared Thus, epothilone A in acetone containing trifluoroacetic acid was heated overnight at 50° and the reaction mixture was adjusted to pH 7 with 1 M phosphate buffer to give 2 isomers, each in 19% yield.

IT 191105-88-1P
RL: AGR (Agricultural use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone derivs. as agrochems. and pharmaceuticals)

RN 191105-88-1 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),6E,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 27 THERE ARE 27 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	130.76	516.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-16.15	-16.15

STN INTERNATIONAL LOGOFF AT 10:13:55 ON 04 JUN 2010